

ANTECEDENTS AND POSTCEDENTS OF TEMPTATIONS DURING SMOKING
CESSATION:
AN ECOLOGICAL MOMENTARY ASSESSMENT STUDY

by

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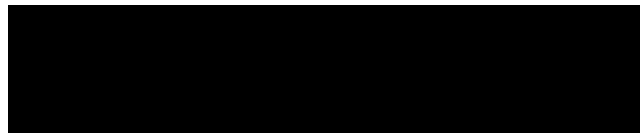
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ABSTRACT

Antecedents and Postcedents of Temptations During Smoking Cessation: An Ecological Momentary Assessment Study

John Lammers, MS, 2018

Dissertation directed by: Andrew J. Waters, Professor, Department of Medical and
Clinical Psychology

Cigarette smoking is the leading cause of preventable death in the U.S. Most cigarette smokers want to quit but are unable to do so. A better understanding of the psychological processes underlying relapse may lead to better interventions. Theory and data suggest that cognitive biases, including attentional bias, may elicit craving and temptations to smoke, and undermine cessation attempts. However, few studies have examined these relationships in the field and none have examined the time course of these relationships. This study used ecological momentary assessment (EMA) to examine the relationship between attentional bias and temptations/craving during the first week of a quit attempt. Participants ($n=119$) carried around a Personal Digital Assistants (PDAs) for one week and completed a smoking Stroop task and a self-report measure of attentional bias at random times (random assessments; RAs), and at temptation episodes (temptation assessments; TAs). The overall goal was to examine the association between attentional bias and temptations/craving.

Specific Aim 1 examined the relationship between attentional bias & Assessment Type during attempted abstinence from smoking. Specific Aim 2 examined whether attentional bias was elevated prior to temptations. Specific Aim 3 examined whether attentional bias was elevated after temptations. Exploratory analyses examined associations between attentional bias and craving, relapse status, and race.

For Specific Aim 1, self-reported attentional bias (but not the smoking Stroop effect) was higher at TAs than RAs. For Specific Aim 2, there was little evidence that attentional bias was elevated in the hours before a temptation. For Specific Aim 3, self-reported attentional bias was elevated at RAs occurring in the 4 hours after a TA. Lagged analyses revealed that self-reported attentional bias predicted craving at the next assessment, and vice versa. Self-reported attentional bias was generally higher in individuals who had relapsed at the end of study, and the smoking Stroop effect was higher at TAs (but not RAs) in participants who relapsed during the first week (compared to abstainers). Overall, there was evidence that self-reported attentional bias provoked craving, and that temptations/craving provoked self-reported attentional bias. In addition, both self-reported attentional bias and the smoking Stroop task may be useful for identifying individuals at risk of relapse.

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CHAPTER 1: INTRODUCTION

CIGARETTE SMOKING

Cigarette smoking is currently the leading cause of preventable death and disease in the United States (Office of the Surgeon General, 2014). Since the surgeon general's report in 1964, scientific research has linked cigarette smoking to a variety of serious health conditions as well as death (Centers for Disease Control and Prevention, 2016; Office of the Surgeon General, 2014; U.S. Department of Health and Human Services, 2004; Xu, Bishop, Kennedy, Simpson, & Pechacek, 2015). Considerable effort has been made to prevent and ultimately reduce cigarette smoking. Despite these efforts, approximately 4,000 people smoke their first cigarette each day in the United States (Office of the Surgeon General, 2014), and most attempts to quit smoking end in failure (U.S. Department of Health and Human Services, 2004).

A better understanding of the psychological processes underlying relapse may lead to better interventions. Theory and data suggest that cognitive biases, including attentional bias, may provoke craving and temptations to smoke, which may in turn undermine cessation attempts. While many laboratory studies have examined these phenomena, few studies have been conducted in the natural environment and none have examined the time course of these relationships in this context. The current study used ecological momentary assessment (EMA) to examine the relationship between attentional bias and temptations/craving during the first week of a quit attempt.

The background material for this dissertation is organized as follows. Chapter 1 reviews the literature on the health effects of smoking and smoking cessation, and the available treatment options for nicotine addiction. Chapter 2 reviews literature on

psychological theories of nicotine addiction, with particular focus on Robinson and Berridge's Incentive Sensitization Theory (1993), which is most germane to the current dissertation study. Chapter 3 reviews the use of Ecological Momentary Assessment (EMA) to examine psychological processes in relapse. Chapter 4 reviews the literature from laboratory and EMA studies that has examined relationships between attentional bias and craving. Chapter 5 reviews three preliminary studies that are pertinent to current dissertation study, describes the rationale for the dissertation study, and presents the Specific Aims. Some of the content of this background material was previously described in Lammers (2017) which examined the associations between stress/negative affect and temptations using the same dataset.

Health Consequences of Smoking

The 1964 report by the United States Surgeon General is considered to be one of the first major public statements supported by scientific research that condemned smoking due to its negative health consequences (Office of the Surgeon General, 2014). Cigarette smoking is known to cause or be associated with numerous negative health conditions and diseases including multiple types of cancers, coronary heart disease, emphysema, stroke, diabetes and chronic obstructive pulmonary disease (Novello, 1990; U.S. Department of Health and Human Services, 2004, 2006, 2012).

Since the first surgeon general report over 40 years ago outlining the negative health effects of smoking, an estimated 12 million people have died from smoking related illnesses (U.S. Department of Health and Human Services, 2004). An estimated 443,000 people die each year due to smoking related diseases in the United States which makes

smoking the largest single contributor to preventable death. (Office of the Surgeon General, 2014).

Smoking cigarettes is harmful to the individual smoker and there are also associated risks to others in the immediate environment and to developing fetuses. Exposure to second-hand smoke in one's environment is associated with increased risk of diseases including heart disease, cancer, and respiratory disease (U.S. Department of Health and Human Services, 2006). Smoking while pregnant is associated with increased risk of miscarriage, low birth weight, and other birth complications (U.S. Department of Health and Human Services, 2004).

Cigarette smoking within the military presents unique risks and is an area of concern. Current rates of smoking are higher in the military compared to the civilian population. Approximately 24% of active duty military members in the U.S. are current smokers compared to 21% of the civilian population ages 18-65 (The Department of Defense, 2013). Smoking undermines an individual's health and readiness degrading their work performance which can jeopardize overall unit effectiveness.

Smoking Prevalence and Monetary Impact

In spite of the overwhelming evidence outlining the risks associated with smoking, approximately 43 million people smoke cigarettes in the United States with an estimated 4,000 people trying cigarettes for the first time each day (Office of the Surgeon General, 2014; U.S. Department of Health and Human Services, 2004).

As noted above, negative effects of smoking can also impact others in the nearby environment. Second-hand smoke contributes to the deaths of approximately 42,000 people in the United States each year (Centers for Disease Control and Prevention, 2016).

Smoking related sickness and death is also expensive totaling an estimated \$156 billion in lost productivity and \$170 billion in directed medical expenses each year (Office of the Surgeon General, 2014; Xu et al., 2015).

Health Consequences of Smoking Cessation

Smoking cessation has been shown to have immediate and long-term health benefits including reducing the risk of suffering a stroke, reducing the risk of developing numerous types of cancers, and reducing the risk of developing coronary heart disease (U.S. Department of Health and Human Services, 2004). Perhaps most importantly, individuals who quit smoking live longer than those who continue to smoke (Centers for Disease Control and Prevention, 2016). Unfortunately, cessations rates are low despite the development of cessation interventions including pharmacological, psychological, and self-help treatments. Even though three out of four smokers report that they would like to quit, less than 5% of people who attempt to quit smoking remain abstinent for greater than 3 months (U.S. Department of Health and Human Services, 2004). Approximately one third of smokers who quit for a year will relapse back to smoking (U.S. Department of Health and Human Services, 2004).

NICOTINE ADDICTION

The addictive properties of nicotine make smoking cessation and maintenance of cessation a difficult process. The addictive qualities of nicotine have been extensively studied and have been implicated as a major factor in tobacco dependence and with difficulty in achieving and maintaining abstinence. Relevant research on the addictive nature of nicotine and cigarettes is reviewed below.

Studies have investigated the acute pleasurable (hedonic) as well as cognitive effects of smoking and nicotine. These studies have investigated different methods of nicotine administration, including inhalation, intravenous, and transdermal. Nicotine absorbed from cigarette smoke (inhalation) has been linked to subjective and objective improvements in both attention and memory (Heishman, Kleykamp, & Singleton, 2010). A meta-analysis of 41 double-blind, placebo controlled studies found evidence for cognitive enhancing effects of smoking including improved attention and memory (Heishman et al., 2010). A literature review on the acute subjective effects of nicotine and smoking demonstrated that individuals report acute hedonic effects from nicotine and smoking (Kalman, 2002). Additionally, reduction of negative affect is commonly reported as a benefit of smoking (Baker, Brandon, & Chassin, 2004). In sum, smokers report or experience many acute benefits from smoking that may contribute to smoking maintenance and undermine cessation efforts.

Nicotine Withdrawal

Nicotine dependence is characterized by tolerance to nicotine and experience of withdrawal symptoms during periods of abstinence (American Psychiatric Association, 2013). Nicotine dependence develops following repeated exposure to nicotine within distinct period of time (Baker et al., 2004). Following the development of dependence, self-administration of nicotine is required to stave off the negative effects of withdrawal. If nicotine intake is too low, a dependent individual will experience withdrawal symptoms including negative changes in mood (e.g. irritability, frustration, agitation), negative physical symptoms (e.g. gastro-intestinal complaints, headaches), and negative cognitive symptoms (e.g. difficulty concentrating). Additionally, individuals undergoing

withdrawal may experience weight gain, disruption in sleep, and increased craving for nicotine that can last for weeks or months (Baker et al., 2004). The discomfort experienced during withdrawal has been considered to be a major contributor to relapse and smoking maintenance. Simply put, cessation attempts fail due to individuals relapsing to smoking to reduce or eliminate these negative symptoms (Robinson & Berridge, 1993).

Treatments for Nicotine Addiction

As noted above, most smokers want to quit. Smokers undergoing a quit attempt may do so utilizing pharmacological and/or behavioral interventions. Nicotine replacement therapy (NRT) is a type of pharmacological treatment used to aid smokers undergoing a quit attempt. NRT is not a single treatment and consists of various products including transdermal patches, lozenges, gum, nasal spray, and oral inhaler which all contain specific levels of nicotine (U.S. Food and Drug Administration, 2010). These treatments are intended to work by replacing the nicotine a smoker typically obtains from cigarettes and then reducing the amount of nicotine ingested over time in order to reduce negative withdrawal effects and their dependence on nicotine (Ehrman et al., 2002). A Cochrane review of all types of NRT currently available indicate use of NRT improves cessation rates by 50-70% compared to smokers who attempt to quit unaided (Stead et al., 2012).

Bupropion and varenicline are two FDA approved cessation medications developed to improve rates of quitting (U.S. Food and Drug Administration, 2010). Unlike NRT, these medications do not contain nicotine. The effectiveness for bupropion was found to be similar to NRT and medication adherence was considered good due to

the low incidence of significant negative side effects (Hughes, Stead, Hartmann-Boyce, Cahill, & Lancaster, 2014). Varenicline has been shown to improve cessation rates compared to control groups receiving no medication and is more effective in extended treatments compared to bupropion (Hajek et al., 2013).

Research studies of psychological and behavioral intervention programs indicate they improve the odds a smoker will quit compared to non-treatment control groups. A review of counseling programs targeting tobacco cessation have shown individual counseling is effective in assisting smokers to quit (Lancaster & Stead, 2008). These findings were consistent with the clinical practice guidelines published by the U.S. Public Health Service which recommends utilizing intensive counseling for smoking cessation (U.S. Department of Health and Human Services, 2008).

Despite the development of effective pharmacological and behavioral interventions, over half of all smokers undergoing a quit attempt do so unaided (self-quitters) (Chapman & MacKenzie, 2010). Of those self-quitters, only 3-5% were found to be abstinent at 12-months after their quit date (Hughes, Keely, & Naud, 2004).

In summary, most smokers report the desire to quit, and there are effective pharmacological and behavior intervention programs that assist individuals in quitting. Yet most people choose to quit unaided with poor overall cessation rates.

Race and Smoking

The current study enrolled a large proportion of African American smokers. Therefore, a brief review of smoking in African Americans will follow. Research investigating racial disparities of smoking and cessation has found significant differences among racial groups. Compared to white smokers, minority smokers have lower rates of

cessation despite being more likely to be light or intermittent smokers (Trinidad, Perez-Stable, White, Emery, & Messer, 2011). African-American smokers are approximately 50% less likely to be successful in quitting compared to non-Hispanic White smokers (Trinidad et al., 2011). Research investigating factors underlying these disparities has found several factors that may contribute to lower cessation rates in minority populations including being less likely to have complete smoking bans at home, being less likely to be advised to quit smoking by a health care professional, and being less likely to utilize smoking medications and NRT (Trinidad et al., 2011). Further research investigating the causes of lower cessation rates is necessary since minority smokers experience a greater level of adverse health effects from smoking compared to non-Hispanic White smokers (Trinidad et al., 2011)

Summary

In summary, cigarette smoking remains a significant public health problem. Most smokers want to quit. However, despite the presence of efficacious smoking cessation therapies, most smokers attempt to quit on their own, and most quit attempts end in failure. Relapse rates are particularly high for minority smokers. A better understanding of the psychological processes underlying smoking cessation and relapse may lead to better interventions. The next chapter reviews some pertinent literature on the psychological processes underlying relapse.

CHAPTER 2: PSYCHOLOGICAL PROCESSES UNDERLYING RELAPSE

As noted in the previous chapter, a better understanding of the psychological processes underlying relapse may lead to better interventions. A review of theories pertaining to relapse will be reviewed next. Major theories of addiction and relapse include positive reinforcement theory, negative reinforcement theory, and, most pertinent to the current study, incentive-sensitization theory.

POSITIVE REINFORCEMENT THEORY

Positive reinforcement theory of drug use is based on learning and conditioning principles where individuals initiate and maintain drug use due to the positive rewards resulting from drug use (Wise & Koob, 2014). Smokers report experiencing various rewards from smoking including improved mood, attention, and concentration (Heishman et al., 2010). Through classical conditioning, smoking cigarettes becomes associated with these rewards. However, it has been noted that while positive reinforcement may play a role in smoking, it is unlikely to be sufficient in maintaining addiction as the acute effects of smoking are relatively modest (compared to other drugs of abuse) and the pleasure experienced may decrease over time due to tolerance (Wise & Koob, 2014).

NEGATIVE REINFORCEMENT THEORY

In contrast to positive reinforcement, negative reinforcement theory indicates that individuals use drugs primarily to avoid unpleasant affective, cognitive and physical withdrawal symptoms (Wise & Koob, 2014). As noted earlier, when abstaining from smoking, regular smokers typically experience several negative withdrawal symptoms including irritability, difficulty concentrating, and increased cravings when they abstain

from smoking (American Psychiatric Association, 2013). Smoking will relieve these symptoms, a form of “escape behavior”, and smoking consistently throughout the day prevents an individual from experiencing withdrawal in the first place. Smoking may also be negatively reinforcing if it removes negative affect caused by another (non-withdrawal related) source (Baker et al., 2004).

However, some researchers have argued that negative reinforcement is unlikely to provide a complete account of tobacco addiction (Robinson & Berridge, 1993). For example, human and animal studies of addiction have shown individuals will reinitiate drug use even after withdrawal symptoms have subsided (Shaham, Shalev, Lu, De Wit, & Stewart, 2003). Most importantly, at many episodes of relapse, individuals report being in a good (or neutral) mood, meaning that there is no negative state to alleviate through smoking (Shiffman, Paty, Gnys, Kassel, & Hickcox, 1996). It is difficult to understand how negative reinforcement accounts for relapse when individuals are not experiencing any withdrawal or negative affect. Moreover, negative reinforcement does not easily account for drug use initiation (Wise & Koob, 2014).

INCENTIVE-SENSITIZATION THEORY

In the Incentive-Sensitization Theory (IST 93), Robinson and Berridge present a biopsychological theory of addiction (Robinson & Berridge, 1993). IST 93 outlines three major features of addiction including drug craving, tendency to relapse back to drug use both early in the quitting process and after long periods of abstinence, and the relationship between drug Wanting and drug Liking (Robinson & Berridge, 1993).

The authors provide significant detail on the neurobiological changes or adaptations that occur after repeated drug use and contend it is these drug-induced

changes of neural circuits that result in significant craving and relapse (Robinson & Berridge, 1993). Craving has been defined as “a strong desire or sense of compulsion to take the drug” by the International Classification of Diseases (World Health Organization, 2016). The Incentive-Sensitization Theory is named due to idea that it is the *sensitization* of neural pathways and the enhanced incentive value assigned to drugs and drug cues that underlies addiction (Robinson & Berridge, 1993). It is hypothesized that the neural pathways become sensitized through drug taking which influences the process of assigning or attributing incentive salience to the mental representations of drug cues (Robinson & Berridge, 1993).

More specifically, according to IST 93, under normal circumstances, a stimulus is processed by one brain system, the “Pleasure Integrator”, and identified as a pleasant stimulus. This process leads to Liking. The Liking system (Pleasure Integrator) communicates with a Wanting system that a pleasurable stimulus has been identified. An “Incentive Salience Attributor” interacts with another mechanism, termed “Associative Learning” by IST 93, and the end result of this processing is that incentive salience is assigned to the mental representations of stimuli paired with pleasure. When this attribution of incentive salience occurs, these “incentive stimuli” provoke Wanting. That is, the Wanting system mediates “subjective craving”, attentional bias, and consumption (Robinson and Berridge, 1993).

Usually, incentive salience is only assigned to stimuli that are associated with pleasurable outcomes. However, Robinson and Berridge (1993) argue that drugs, including nicotine, can cause neuroadaptations that give rise to an attribution of incentive salience (Wanting) without pleasure. After repeated drug use, “sensitization” occurs in

some individuals (as noted above, this is why the theory is termed “incentive sensitization” theory), with the result that drugs, and drug-related cues are craved more than would be expected based on levels of Liking.

Furthermore, according to IST 93, drug Liking *decreases* as drug Wanting *increases*. Wanting increases due to incentive sensitization, as just described. IST suggests that there is tolerance (not sensitization) to drug Liking over time. After repeated drug administration, individuals typically experience tolerance to that amount of drug and experience less pleasure with each subsequent administration. It becomes necessary to consume greater amounts of the substance to experience a similar effect. This is why some addicted individuals report that they used to find drugs pleasurable, but they no longer do so – but they still want them! Therefore, although Wanting and Liking usually go together (in non-addicted individuals), they are considered separate experiences for those with drug addictions (Robinson & Berridge, 1993).

Wanting versus Liking

As just noted, repeated pairing of drug cues with drug use over time increases the attractiveness of drug-associated stimuli and increases a person’s Wanting for drugs (Robinson & Berridge, 1993). IST 93 is clear that Wanting is not the same as Liking. This distinction is discordant with other theories of addiction that hypothesize that it is drug Liking and the desire to experience the pleasurable subjective effects of drugs which serves as the primary motivation for drug-seeking and drug-use behavior (Robinson & Berridge, 1993).

Tibboel et al. (2015) have reviewed the literature that demonstrates the separability of Wanting and Liking. Because Liking is not a focus of the current

dissertation study, this literature is not reviewed here. However, both animal and human studies have provided evidence that Wanting can occur without Liking, and Liking can occur without Wanting (Tibboel, De Houwer, & Van Bockstaele, 2015).

Most pertinent to the current dissertation is the idea that the Wanting system is more important in addiction than the Liking system, and the notion that Wanting is associated with attention to drug cues (“attentional bias” to drug cues). As Berridge (2009) notes:

....incentive salience transforms the mere sensory shape, smell or sound into an attractive and **attention-riveting** incentive. Once attributed, the incentive percept becomes difficult to avoid noticing, the eyes naturally move toward the incentive, it captures the gaze and becomes motivationally attractive, and the rest of the body may well follow to obtain it. (p. 2)

As can be seen, IST gives attentional bias a prominent role. However, IST does not describe in detail the proposed causal relationships between attentional bias and craving. Rather, attentional bias and craving were viewed by IST as two indices of a Wanting system. However, this idea was further developed by Franken (2003) and is reviewed in Chapter 4.

Neurobiology of Wanting and Liking

IST 93 explained that addiction developed due to adaptations of neurobiological pathways responsible for Liking and Wanting. A detailed account of the neurobiological processes underlying Liking and Wanting is beyond the scope of this manuscript. However, a brief review is presented below.

IST 93 noted that all drugs of addiction activate the dopamine system. Although dopamine transmission in the mesolimbic system had historically been associated with pleasure (liking), IST 93 conceptualized dopamine transmission as mediating the process of attribution of incentive salience (described earlier). With continued drug use, dopamine transmission is increased over time (sensitization), and this process underlies sensitization of incentive salience.

In a more recent review, Berridge (2009) elaborated further and wrote that “different brain mechanisms seem to mediate wanting and liking for the same reward.” Berridge (2009) noted that there is an area of the nucleus accumbens that is part of the Liking pathway that acts as a “hedonic hotspot” and other regions in the nucleus accumbens that act as part of the Wanting pathway. Relatedly, some research has drawn a distinction between the “core” and the “shell” of the nucleus accumbens. Pecina and Berridge (2000) identified a “liking hotspot” on the “shell” of the nucleus accumbens that appeared to increase “liking” behavior. This same reaction was not found when areas of the “core” were tested (Pecina & Berridge, 2000). The main idea emerging from this area of research is that the mesolimbic dopamine system is associated with Wanting, whereas Liking is mediated by activity in more restricted subcortical “hedonic hotspots”. In addition, Tibboel et al. (2015) note that opioid transmission is more closely associated with Liking than Wanting.

STRESS/NEGATIVE AFFECT

In the following sections, research examining the relationship between stress/negative affect and craving will be reviewed. Although stress and negative affect are not the central focus of the current dissertation, this review is provided for the

following reasons. First, stress and negative affect have been identified as major factors contributing to relapse (Shiffman & Waters, 2004), and therefore, they are important to review. Second, stress and negative affect were examined in a preliminary study that is germane to the current study, as described later (Lammers, 2017).

A meta-analysis of 27 studies examined how manipulations of negative affect and positive affect influence subsequent craving to smoke (Heckman et al., 2013). When manipulating negative affect, researchers generally found increases in post-manipulation craving (with a medium effect size) (Heckman et al., 2013). However, manipulating positive affect did not result in changes in craving. The meta-analysis lends support to theories of smoking involving negative affect and are consistent with smoker's self-reports that increases in negative affect contribute to subsequent smoking (Heckman et al., 2013).

Despite the results of the meta-analysis reported by Heckman et al. (2013), not all studies examining smoking have shown increases in craving following manipulation of negative affect. In a study conducted by Shiffman and colleagues (2013), craving was not increased following exposure to cues that increased negative affect. This could be due to the relatively short time period between negative cue exposure and ad lib smoking opportunity (Shiffman et al., 2013).

Cue exposure ("imaginal" and "in-vivo") paradigms have also been used to manipulate craving and to examine the effect of this manipulation on stress and negative affect. In these types of studies, participants are exposed to cues that either elicit craving (drug cues) or cues that are not intended to elicit craving (neutral cues). Researchers then measured subsequent changes in stress and negative affect. In one illustrative study,

participants reported significant greater craving following exposure to drug cues (Drobes & Tiffany, 1997). Increases in craving did not differ between imaginal or in-vivo scenarios. This study also demonstrated that the craving manipulation produced increases in negative affect and decreases in positive affect in a laboratory setting. (Drobes & Tiffany, 1997). Taken together, Heckman et al. (2013) and Drobes and Tiffany (1997) demonstrate that negative affect can increase craving, and that craving can increase negative affect.

Ecological Momentary Assessment (EMA) has been used to examine the relationship between stress/negative affect and craving. EMA will be described in more detail in the following chapter, but a few key findings relating to stress/negative affect will be briefly reviewed here. Researchers examined differences in negative affect, craving, and urge at multiple assessments (random assessments, temptation assessments, and lapse assessments) during cessation attempts (Shiffman, Gnys, et al., 1996). Higher levels of urge and craving were reported during the time periods just prior to temptation assessments (Shiffman, Paty, et al., 1996). Negative affect was also higher just prior to temptation episodes. Similarly, negative affect was found to be highest just prior to just prior to lapse assessments (Shiffman, Paty, et al., 1996).

Recent EMA studies have examined changes in craving and mood resulting from manipulations in cue type (either neutral or smoking). A cue reactivity EMA (CREMA) study by Warthen and Tiffany (2009) found significant increases in craving following exposure to smoking-related cues but not neutral cues in the field. Following exposure to smoking cues, there were significant increases in negative mood and decreases in positive mood. In this study, method of exposure produced significantly different results with

smoking-related photographs producing a larger change compared to imagery scripts (Warthen & Tiffany, 2009).

A similar CREMA design was utilized to determine how exposure to cues (either photographic or in-vivo) impacted subsequent craving and mood (Wray, Godleski, & Tiffany, 2011). Similar to the study above, both smoking cues produced higher craving and significantly worse mood compared to neutral cues (Wray et al., 2011).

Lammers (2017) reported the results of another EMA study that investigated the timeline of stress and negative affect before, during, and after temptation episodes. This study will be reviewed in the “preliminary studies” section. In general, both laboratory and EMA studies have provided support for the hypotheses that stress/negative affect increases craving (or elicits temptations) and that craving increases stress/negative affect.

The following chapter describes EMA methodology in further detail, including its use for the assessment of attentional bias in the field.

CHAPTER 3: ECOLOGICAL MOMENTARY ASSESSMENT

INTRODUCTION TO EMA

Ecological Momentary Assessment can be best understood by examining each of its terms. The first term, “Ecological,” is related to the naturalistic setting in which participants contribute data. Compared to laboratory studies, participants complete assessments in their normal environments which presumably produces “ecologically valid” data. The second term, “momentary,” is related to the time period of the assessment. Participants are typically instructed to respond based on how they feel in that moment (or very recent past) compared to attempting to recall their experiences during a more distant past time period. In other words, participants are not asked to think about how they felt in the past but rather they are probed with how they are feeling at the time the assessment is administered. The last term, “Assessment” refers to the multiple times a person contributes data throughout the study. The addition of repeated sampling produces rich datasets with greater external validity compared to laboratory studies (Shiffman, Stone, & Hufford, 2008)

The development of new tools and technologies has allowed for EMA studies to evolve from relying on paper and pencil self-report measures assessing a few aspects of an individual’s experiences to using electronic devices capable of assessing multiple types of variables. Currently, PDAs have largely been replaced by utilizing smartphones (either provided by the researchers or by adding a program to the participant’s own phone) to gather data in their natural environments at multiple time points throughout the day (Shiffman et al., 2008). Related to the current dissertation, past EMA studies have investigated how psychological variables are related to temptation and relapse. EMA

design is particularly well-suited for studying addiction and relapse because it is capable of assessing changes over time of multiple variables of interest related to drug use.

In sum, EMA methodologies have greater external validity, gather large data sets composed of multiple sampling points, produce data depicting changes in variables over time, and can extend research previously conducted in the laboratory setting (Shiffman et al., 2008). Shiffman, Stone, and Hufford (2008) review the history and suitability of EMA as a type of study design, and relevant background information is contained below.

Assessment Schedules

Researchers utilize different types of assessment depending on the variables and relationships of interest (Shiffman, 2009). Assessment schedules can be separated into two main types, either event-based or time-based. When utilizing an event-based assessment schedule, participants are instructed to self-initiate an assessment each time they experience a pre-defined event or situation (Shiffman et al., 2008). Examples of these events include the experience of temptation, exposure to drug cues, use of a substance, after waking, or after eating a meal (Shiffman, 2009). Utilizing event-based assessment schedules allows researchers to gather information about internal and external factors that occur in a similar time period as the pre-defined event of interest.

Time-based schedules are the second major type of assessment schedule used in EMA studies. While time-based assessment schedules can vary greatly, they generally consist of either fixed-interval or random-interval schedules. An example of a fixed-interval schedule would be when an assessment is presented at pre-determined four hour intervals during waking hours (Shiffman et al., 2008). An example of a random-interval schedule is when a PDA or smartphone is programmed to present four assessments each

day at random times through the day. Compared to event-based assessments, time-based assessments gather information regarding the changes in subjective and objective variables throughout the day. Information gathered from time-based schedules serve to provide information on how fluctuations in psychological variables (e.g. mood and cognition) are associated with subsequent behaviors and outcomes (Shiffman, 2009). EMA studies may also utilize a mixture of both event-based and time-based assessments (as was done in the current dissertation study).

EMA and Addiction

In the domain of addiction, it can be difficult to study some variables of interest, such as temptation and relapse, using traditional laboratory research methods. As previously mentioned, EMA addiction studies are not reliant on retrospective recall and are capable of gathering information at multiple time points each day. This allows for detailed examination of factors over time that are associated with addiction (Serre, Fatseas, Swendsen, & Auriacombe, 2015; Shiffman, 2009). EMA researchers are able to gather information on multiple factors underlying drug use including affect, craving, stress, mood, and environmental information (Shiffman, 2009).

Protocol adherence is an important factor in all studies and is especially important in EMA studies as participants complete assessments without the supervision of researchers. Additionally, individuals with drug addictions may have generally unstable life circumstances that could potentially impact data collection (Shiffman, 2009). That being said, past studies of addiction utilizing EMA methodologies and gathering data with handheld electronic devices have found appropriate protocol adherence from

participants with varying types of addictions(e.g. crack-cocaine, opiate, and heroine) (Shiffman, 2009).

EMA and Cigarette Smoking

Numerous EMA studies have investigated cigarette smoking. An illustrative study was conducted by Shiffman and Waters (2004). Individuals undergoing a cessation attempt completed event-based and time-based (random interval) assessments. Participants were instructed to initiate an assessment during periods of significantly heightened temptation and also if they lapsed back to smoking. A measure of negative affect was administered during every assessment (Shiffman & Waters, 2004). The researchers were interested in the immediate precipitants of lapse episodes, particularly regarding whether negative affect was elevated in the days and hours prior to relapse. Data collected were capable of detecting hour to hour increases in negative affect prior to some first lapse episodes. In contrast, more distal ratings and daily ratings of negative affect were not prospectively associated with relapse (Shiffman & Waters, 2004). This finding underscores the importance of examining within-day changes in psychological variables.

EMA and Temptations/Craving

In the current dissertation study, participants were instructed to enter a temptation episode when they experienced a temptation to smoke. The definition of temptation was adapted from Shiffman et al. (1996) and was defined as “felt an acute increase in the desire to smoke, or an occasion when they felt they came to the brink of smoking without actually smoking.” Therefore, as noted by Lammers (2017), elevated “desire” (i.e. urge), which is very highly correlated with “craving” (Shiffman et al., 1997), is part of the

definition of a temptation. Therefore, the expectation is that participants would report much higher craving at TAs than RAs, and has been observed in the past (Lammers, 2017; Shiffman, Paty, et al., 1996).

Nonetheless, although participants report more craving at TAs than RAs, temptations, as defined above, are not coterminous with high craving. Theoretically, part of the definition of temptation involves the perception that one has “come to the brink of smoking” without actually doing so. The sense of being on the point of acting may occur in the absence of craving. For example, Berridge (2009) argued that incentive salience may be assigned to the mental representations of drug-related actions (“action salience”) as well as the mental representations of drug-related stimuli (“incentive salience”), and the latter may be more strongly related to subjective craving. As Berridge (2009, p. 9) notes, an addict “might urgently “want” to act.” The attribution of incentive salience to stimuli and actions might take place together with the attribution of “action salience” occurring in the absence of subjective craving (Berridge, 2009).

Empirically, some TAs are entered that have low levels of craving. For example, in a large dataset collected by Shiffman et al. (1996), craving of “0” or “1” (on a 0-10 scale) was endorsed on 18% of TAs (Shiffman, email communication, 9/24/16). Similarly, in the dataset used by Lammers (2017), ~22% of TAs had a craving level of “1” (1-7) scale, and in a study of alcohol-dependent participants, ~60% of TAs had a craving level of “1” on a 1-7 scale (Snelleman et al., 2018). Although it is possible that such entries are due in part to measurement error, it seems likely that subjects do indeed experience some temptations when experiencing little or no craving. Relatedly, EMA

research indicates 7% of first *lapses* to smoking occurred when little or no craving was reported (Ferguson & Shiffman, 2010).

In sum, although elevated craving is often reported at temptations (when compared to RAs), one can argue that temptations and craving are theoretically and empirically distinct. Given that temptations are discrete episodes, it is easy to examine the time course of attentional bias before, during, and after these episodes. Examination of these relationships will be the focus of the specific aims of the study. Nonetheless, given the overlap between temptations and craving (when assessed on a continuous scale), the association between attentional bias and craving will also be examined in exploratory analyses, described in more detail later.

Methodological Issues with Assessment of Temptations

As noted by Shiffman et al. (2008), an important limitation in the use of event-based monitoring, such as monitoring of temptation episodes, is that it is difficult to verify compliance. For example, it is difficult to know whether a participant made entries for all his or her temptation episodes, and, if not, whether the temptation episodes were “representative” of his or her “population” of temptation episodes. Whereas entries of smoking/lapse episodes can sometimes be confirmed by biochemical measures (e.g., Shiffman & Paty, 2003), this approach is not possible for temptation episodes.

Nonetheless, Shiffman (2009) notes that subjects in EMA studies do record multiple temptations (sometimes more than 200; Tindle, Shiffman, Paty, & Dang, 2006). Moreover Shiffman et al. (1996) reported that temptation episodes were different from random assessments on some variables (e.g., higher negative affect at temptations than random assessments) and also differed from assessments at lapse episodes. This pattern

of data helps to bolster the case that the entered temptation episodes are different from randomly selected moments in a manner consistent with predictions.

As noted above, it is difficult to validate temptation entries against a second report. During an EMA protocol, Litt et al. (1998) asked alcohol-dependent participants to complete an assessment “whenever they experienced a ‘noticeable increase’ in their desire to drink” (p. 49). Although few details were provided in Litt et al. (1998), it appears that participants were also queried at the end of each day as to how many urges (and drinking episodes) they experienced each day. All responses were made on 5- × 7-in. record cards. Litt et al. (1998) reported that participants initiated a recording upon the conscious urge to drink (or actual drinking) “on just 71 occasions overall, whereas end-of-day reports indicated that urges occurred on over 350 occasions in 21 participants” (p. 50). Taken at face value, this report indicates that participants rarely completed urge assessments (which are similar to temptation assessments) during EMA. However, this study focused on alcohol use (vs. cigarette smoking), and the findings may not apply to smokers.

Use of EMA to Study Smoking and Cognition

The development of small, personal electronic devices allows for cognitive measures to be administered in a participant’s normal environment outside of laboratory settings. PDAs and smartphones are capable of presenting multiple types of cognitive assessments. A study by Shiffman and colleagues (1995) more than twenty years ago first illustrated that cognitive assessments can be administered on handheld devices. Dependent and non-dependent smokers completed cognitive and subjective measures at multiple prescheduled assessments in their normal environment (Shiffman, Paty, Gnys,

Kassel, & Elash, 1995). The cognitive measures consisted of a simple reaction test and a test of mental arithmetic. Results revealed significant differences in performance between dependent and non-dependent smokers that were consistent with previous laboratory studies (Shiffman et al., 1995). The consistency of these findings indicates using PDAs to administer assessments in a field study is methodologically feasible.

In a study examining the feasibility of administering reaction times tests on PDAs in the field, smokers and non-smokers were recruited to complete assessments over a one-week period (Waters & Li, 2008). The participants completed subjective measures assessing affect, craving, and mood, and contextual measures assessing environmental information. The Classic Stroop, Emotional-Stroop, and Smoking-Stroop tasks were also presented on PDAs. Rate of compliance was good indicating that EMA is a suitable method to gather ecologically valid cognitive data (Waters & Li, 2008). As described in more detail in later sections, numerous other studies have administered cognitive assessments on mobile devices (e.g., Waters, Marhe, & Franken, 2012; Waters et al., 2014).

Reactivity

In order for data obtained in EMA studies to be valid, it is important that participants' thoughts, emotions, or behaviors are not impacted by the act of completing assessments. In the EMA literature, the notion that the act of assessment itself causes changes in the processes being measured is termed "reactivity" (Shiffman et al., 2008). As noted by Shiffman et al. (2008), based on the self-monitoring literature, it is not unreasonable to be concerned that EMA may itself cause changes in behavior (rather than just assessing behavior). In the smoking literature, some early studies examined variables

that moderate the effect of self-monitoring on smoking behavior. For example, in one study, self-monitoring reduced smoking in the group that was motivated to quit but not in the unmotivated group (Lipinski, Black, Nelson, & Ciminero, 1975).

In another study of smokers preparing for a quit attempt, self-monitoring of cigarette consumption during a demanding EMA protocol only decreased smoking by 0.3 cigarettes per day while CO levels remained unchanged (Shiffman et al., 2002). Reduction in cigarette smoking reached statistical significance but did not equate to clinically significant reductions in consumption.

More recent studies have examined the effect of “assessment frequency.” Researchers manipulated the number of the random assessments participants were required to complete to determine if assessment frequency influenced subjective reports and behavior. In study of chronic pain, the number of assessments completed per day was manipulated in order to understand how assessment frequency impacts participants’ subjective responses (Stone et al., 2003). Participants were randomly assigned to one of four groups that differed on the number of assessments they were required to complete each day. There was no significant effect of assessment frequency on self-reported pain, suggesting that reactivity was unlikely to play a large role in that context (Stone et al., 2003).

A recent study manipulated the number of EMA assessments completed each day by cigarette smokers undergoing a cessation attempt to determine if assessment frequency (low-1/day vs. high- 6/day) affected short-term abstinence, long-term abstinence, and subjective measures (McCarthy, Minami, Yeh, & Bold, 2015). There was no significant effect of assessment frequency on short- or long- term abstinence.

However, lower anxiety, hunger, anger, positive affect, and craving were reported by the high frequency group (McCarthy et al., 2015).

This finding could indicate that the act of frequent assessment during EMA changes participants' subjective experiences. Shiffman (2015) provided a response to the McCarthy et al. study. He first noted that it was important to note that EMA assessment frequency did not influence overt behavior (Shiffman, 2015). Shiffman (2015) also noted that EMA studies generally examine the relationship between variables (such as in the current dissertation study), rather than the "absolute values" or averages of variables. While mean level of response on a number of self-report measures may have been reduced, there is no indication that the relationship between variables has been influenced by assessment frequency (Shiffman, 2015).

Reactivity may also potentially differ by type of assessment (e.g., TA vs RA). For example, the typical participant responds to many more RAs than TAs; it is possible that the reductions in self-reported craving and other measures observed by McCarthy et al. (2015) may be stronger at RAs, as the "frequency" of RA assessment is greater. Moreover, the McCarthy et al. (2015) study did not include cognitive assessments, and so it is unclear how frequent testing could impact cognitive assessments and whether this could differ by assessment type. The validity of the data could potentially be impacted if reactivity influenced responses to TAs and RAs differently, although the author is not aware of any studies that have examined this. If this were shown to be problematic, a study could be designed using only one type of assessment - either self-initiated or random assessments - to obviate this concern.

The following chapter describes research that has examined the association between attentional bias and craving, both in the lab and during EMA

CHAPTER 4: ATTENTIONAL BIAS

INTRODUCTION TO ATTENTIONAL BIAS

Cognitive models of addiction often theorize that addiction involves a conflict between two types of cognitive process. “Automatic” (or “implicit”) processes, generally *increase* the risk of drug taking/relapse, whereas “controlled” (or “explicit”) processes, which attempt to inhibit automatic processes or the output of automatic processes, operate to *decrease* the risk of drug taking/relapse (see review in Stacy & Wiers, 2010).

Automatic processes are relatively fast, parallel, and automatic processes that are outside of one’s conscious awareness (“System 1” in Kahneman’s terminology), whereas controlled processes are slow, reflexive, and serial (“System 2” in Kahneman’s terminology) (Kahneman, 2011). If automatic processes dominate, then drug use/relapse is more likely to occur. If controlled processes win out, then abstinence should be maintained. This framework can be termed “dual-process theory” because of the emphasis on two distinct types of process (Kahneman, 2011).

Two widely studied automatic processes in addiction are attentional bias and approach bias. Attentional bias is generally considered an automatic cognitive process in which a smoker attends to a smoking-related stimulus without making the conscious decision to attend to that stimulus (Field & Cox, 2008). Attentional bias is a focus of this dissertation, and assessments of attentional bias will be described in detail later. Another automatic process is "approach bias" which refers to the tendency to automatically approach drug-related cues (Wiers, Eberl, Rinck, Becker, & Lindenmeyer, 2011). Approach biases, which are not the focus of the current dissertation, can be assessed with computerized tasks that involve motor movements such as the Approach-Avoidance task

(Wiers et al., 2013). Approach bias is present in heavy smokers but not in ex-smokers and research suggests that approach biases in smokers are correlated with craving (Wiers et al., 2013).

THEORETICAL IMPORTANCE OF ATTENTIONAL BIAS

As noted earlier, IST 93 assigned an important role for attentional bias. Specifically, attentional bias is an index of Wanting or sensitized incentive salience, which, according to IST, is the core process in addiction.

Although IST 93 assigned an important role to attentional bias, the authors did not provide a detailed account of the proposed causal relationships between attentional bias craving and drug use. However, Franken (2003) elaborated on Robinson and Berridge's ideas and provided a more detailed model of the proposed causal relationships between these constructs. Most pertinent to the current study, Franken (2003) suggested that excessive attentional bias contributes to increases in craving which, in turn, contributes to excessive attentional bias. That is, there is a bidirectional causal relationship between attentional bias and craving (Franken, 2003).

Thus, in Franken's (2003) model, increases in attentional bias can lead to (or cause) increases in craving. Increases in attentional bias may cause increases in craving due to increases in exposure to drug cues. Thus, an individual with a high attentional bias is more likely to be exposed to smoking cues, which in turn may provoke craving or temptations to smoke (see Figure 1). Conversely, according to Franken (2003), increases in craving (or feeling tempted to smoke) can lead to (cause) increases in attentional bias (see Figure 2). However, Franken (2003) did not elaborate on the underlying mechanisms for the causal relationship between craving and attentional bias.

Franken's (2003) model also predicts that there should be an association between attentional bias and drug use or relapse, partly mediated by craving. Some research, which is described in more detail later, has reported that attentional bias for drug cues has been found to prospectively predict outcome in addictive behavior (e.g. Janes, Pizzagalli, Richardt, deB, et al., 2010; Powell, Dawkins, West, Powell, & Pickering, 2010; Waters, Shiffman, Sayette, et al., 2003). Thus, interventions that reduce or reverse attentional bias may be beneficial in treatment in addictions.

Franken (2003) also notes that attentional bias for drug stimuli, in addition to increasing craving, may also cause an increase in drug-related cognitions. For example, individuals with a high attentional bias may be more likely to retrieve (pleasurable) memories of drug-taking episodes or to ruminate about drug taking. These additional cognitive processes may interfere with working memory or executive function and undermine cessation attempts. However, the assessment of other drug-related cognitions is beyond the scope of this study, which focuses solely on the association between attentional bias and temptations/craving.

Attentional bias has been examined with multiple substances including alcohol, heroin, cocaine, and tobacco in both laboratory and field settings (Field, Munafò, & Franken, 2009). While attentional bias has been studied in addiction research, it is also worth noting that attentional bias also been extensively investigated in relation to the emergence and maintenance of clinical conditions including anxiety and depressive disorders (MacLeod, Mathews, & Tata, 1986).

Assessing Attentional Bias

Given the theoretical importance of attentional bias, it is important to understand how it is assessed. In fact, there are many methods used to assess cognitive biases including reaction time assessments, self-report assessments, the use of eye movements, and measures of brain activity. A comprehensive review of all measure types is outside the scope of this manuscript. The following is a brief review of the most commonly-used assessments.

Reaction Time Assessments

Attentional bias has most commonly been assessed using reaction time tasks derived from experimental cognitive psychology. The two most widely used tasks have been the addiction Stroop task, which is used in the current study, and the visual probe task. These tasks are reviewed below.

In the original “classic” Stroop task, participants are required to name the colors of congruent (e.g., GREEN written in green ink) and incongruent color words (e.g., RED written in green ink) (Stroop, 1935). Participants are typically much faster to color-name congruent than incongruent stimuli, due to the presence of the conflict in the latter. The addiction Stroop tasks involve presenting drug-related and neutral words in different color font (Cox, Fadardi, & Pothos, 2006). Participants are instructed to indicate the color of the word. Typically, addicted individuals, but not controls, are slower to color-name drug-related words than neutral words (Field & Cox, 2008). This difference in processing times is known as the addiction Stroop effect. Processing of the drug-related word interferes with the color-naming task in some way that response times are slower to color-name drug-related words. One advantage of the addiction Stroop is that it is simple

and can be administered on both stand-alone computers as well as hand held devices such as PDAs or smartphones. This will be described in more detail later.

Visual Probe Task

The visual probe or dot probe task is another common task used to assess attentional bias. This task was first developed to measure attentional bias resulting from emotional disorders such as anxiety (MacLeod et al., 1986) but can also be used to measure attentional bias in addiction (Ehrman et al., 2002). To assess attentional bias in addiction, drug-related and neutral words (or pictures) are presented side-by-side on a computer screen, typically for 500 ms. The two pictures are then replaced by a single dot appearing in a location previously occupied by one of the pictures. Participants are required to indicate the location of the dot as quickly and as accurately as possible by pressing one of two response keys. Typically, addicted individuals are faster to indicate the location of a dot that replaces a drug-related stimulus than a neutral stimulus. This difference in response times is the attentional bias measure derived from the VP task (Ehrman et al., 2002). For example, in one of the earliest studies in smokers, current smokers exhibited an attentional bias towards smoking cues, whereas non-smokers did not (Ehrman et al., 2002). As noted later, the visual probe task has also been modified for the use of attentional retraining (attentional bias modification).

Self-report Assessments

Although the cognitive processes which give rise to attentional bias to drug cues are thought to operate rapidly (i.e., within 500 ms) and largely automatically, there is often a conscious “end product” to these automatic processes. For example, a smoker trying to abstain may find him or herself staring at someone smoking, although that

individual would have no insight into the automatic cognitive processes that initially caused the shift of attention. Similarly, on the VP task, the cognitive processes that underlie the shift in attention to the salient stimulus occur too quickly for the involvement of conscious processing (which is typically engaged after 500 ms), but the participant may (consciously) realize that he or she is tending to attend to the salient stimuli as they perform the task.

This raises the question as to whether attentional bias can be assessed using self-report questions, such as “How often have you found yourself staring at cigarettes and cigarette smoke?”. Although self-reported attentional bias is at best a crude outcome measure of underlying automatic processes, self-report measures of attentional bias may have utility in some research contexts (Leventhal, Waters, Moolchan, Heishman, & Pickworth, 2010; Robinson et al., 2015). For example, the 8-item Subjective Attentional Bias Questionnaire (SABQ), has shown favorable psychometrics properties (Leventhal et al., 2010). The SABQ total score (mean of 8 items) was greatly increased by abstinence (effect size Cohen’s $d = 1.23$, $p < .001$), and the abstinence-induced increase in the SABQ was reliably correlated with a measure of tobacco dependence, the Fagerstrom Test for Nicotine Dependence (FTND) ($r = 0.24$, $p < .001$) (Leventhal et al., 2010). In Robinson et al. (2015) Study 2, higher scores on the SABQ assessed in smokers attempting to quit were significantly associated with higher scores on the FTND at three timepoints. Higher scores on the SABQ were also associated with greater attentional bias assessed on the PDA. In that study, SABQ scores were also associated with cessation outcomes, with greater reported attentional bias being associated with a higher risk of relapse at end of treatment (Robinson et al., 2015).

Researchers have also tried to assess attentional bias with a single-item. As described in more detail later, Waters et al. (2014) reported that attentional bias assessed with the smoking Stroop task was associated with self-reported attentional bias assessed with the item “My attention is often drawn to cigarettes” (assessed on a 1-7 scale). The subjects who reported greater self-reported attentional bias also exhibited greater attentional bias on the smoking Stroop task during the first week of a quit attempt (Waters et al., 2014).

Eye Movements and Smoking Cues

Another useful method for assessment of attentional bias is through measuring eye movements (Henderson, Shinkareva, Wang, Luke, & Olejarczyk, 2013). Eye movements provide a direct and objective assessment of attention to smoking cues. Many studies of attention and addiction have included measures of eye movements to assess attentional processes in drug users which serves to compliment data derived from reaction time assessments. In an early study, researchers assessed the visual scanning paths of cocaine dependent participants (Rosse, Miller, Hess, Alim, & Deutsch, 1993). Participants viewed an image of a crack cocaine pipe and a flower for 90 seconds each during a passive viewing procedure. Cocaine dependent participants’ visual scanning paths of the crack pipe more closely resembled the actual image than did the visual scanning paths of the flower. Furthermore, the accuracy of visual scanning discriminated heavy cocaine users from light cocaine users (Rosse et al., 1993).

Eye movements have also been used to study attention to smoking cues. For example, Mogg, Bradley, Field, and De Houwer (2003) examined eye movements in smokers using the visual probe task. The direction of initial orienting and the duration of

eye gaze was assessed. Smokers looked at smoking stimuli longer than neutral stimuli, when compared to non-smokers (Mogg, Bradley, Field, & De Houwer, 2003). Moreover, gaze duration on smoking stimuli correlated with explicit measures of stimuli's affective and motivational valence ratings and with attentional bias assessed using reaction times (Mogg et al., 2003). As noted later, acute abstinence from smoking has been shown to increase attentional bias to smoking cues, as assessed by eye movements (Peucker & Bizarro, 2014).

EMPIRICAL STUDIES

The relationship between attentional bias and craving in addiction has been examined with a number of different designs, as illustrated in Table 1. Some studies have used a correlational design in which researchers have examined the correlation (e.g., using Pearson's r) between attentional bias and craving, either at the same time-point, or at different timepoints. These studies have typically occurred in a laboratory setting (Box 1, Table 1), and they have generally been cross-sectional. However, some studies have examined the correlation between attentional bias and craving assessed in the field (Box 2, Table 1). Due to the correlational nature of the design, one cannot draw strong causal inferences from these studies (i.e., studies in Boxes 1 and 2, Table 1).

Other studies examining the relationship between attentional bias and craving in addiction have used an experimental approach. In some lab studies, attentional bias has been manipulated as an independent variable (using attentional bias modification, or ABM), and the effect on craving (the dependent variable) examined (Box 3, Table 1). In other lab studies, craving has been manipulated as an independent variable (using, for example, a deprivation manipulation), and the effect on attentional bias (the dependent

variable) examined (Box 5, Table 1). Most studies have occurred in the lab (Boxes 3 and 5), although it is possible to conduct studies in the field (Boxes 4 and 6).

The following review examines some selected studies in more detail, with a particular focus on studies conducted in smoking.

CORRELATIONAL STUDIES

Lab Studies (Box 1, Table 1)

This first section will review studies where the researchers examined the correlation between attentional bias and craving. That is, the studies examined whether drug users who exhibited higher levels of attentional bias reported higher levels of craving. These studies are not experimental studies because there is no manipulation of craving or attentional bias (i.e., no random assignment to groups). Selected pertinent studies are summarized in Table 2.

Most importantly, Field et al. (2009) reported a meta-analysis of the association between craving and attentional bias across all addictions. For each study examined, a Pearson's r summarized the association between attentional bias and craving. Crucially, this meta-analysis of 68 independent studies reported a significant association between attentional bias and craving, even after accounting for possible effects of publication bias (Field, Munafò, et al., 2009). Further analyses suggest that the association is larger when craving was high compared to when craving was low. The magnitude of the correlation (between attentional bias and craving) did not differ between treatment-seekers and non-treatment seekers. The material below reviews selected studies from the Field et al. (2009) study and from more recent studies.

In an influential early study, Mogg and Bradley (2002) assessed performance on the smoking Stroop and VP tasks when participants were abstinent from smoking and when they were non-abstinent from smoking. Crucially, self-reported urge (craving) was correlated with attentional bias in both states. This study provided strong evidence for an association between attentional bias and craving in smokers (Mogg & Bradley, 2002).

In a second influential study, VP performance and eye gaze were measured to determine how attentional bias differed between low and moderate dependent smokers (Mogg, Field, & Bradley, 2005). For the present purposes, the main result was that attentional bias was independently associated with self-reported craving (Mogg et al., 2005).

In a cessation study, participants were randomized to either a nicotine replacement therapy (NRT) group or placebo (Waters, Shiffman, Sayette, et al., 2003). In this study, the placebo group reported significantly higher ratings of “urge” to smoke compared to the NRT group. When examining attentional bias, individuals in the placebo group exhibited significantly longer reaction times and committed significantly more errors on the smoking stimuli trials (Waters, Shiffman, Sayette, et al., 2003). However, the correlation between attentional bias and craving was not significant. Since this study was a cessation study, data on relapse after quit day was gathered. A significant relationship was found between Stroop performance and relapse. Analysis indicate the daily risk of relapse increased for every 100 millisecond increase in reaction times and Stroop performance was predictive of abstinence one week post quit-day (Waters, Shiffman, Sayette, et al., 2003).

In another eye movement study (Kang et al., 2012), participants were simultaneously presented with a smoking related and neutral photo. Researchers found a significant bias towards the smoking related photos. Most relevant here, there was also a large significant correlation between attentional bias and craving ($r=.66$) (Kang et al., 2012).

It is worth noting that attentional bias has also been theorized to influence how former smokers attend differently to smoking and neutral cues. Reaction times on the visual probe task were measured in groups of former smokers who differed on length of abstinence (Peucker & Bizarro, 2014). Data indicated those with recent abstinence (<2.5 years) and intermediate abstinence (2.5-10 years) responded significantly slower to smoking cues compared to neutral cues. The authors discussed the possibility that former smokers were able to employ cognitive strategies to attend away from smoking cues (Peucker & Bizarro, 2014).

Field Studies (Box 2)

As described in more detail later (preliminary studies section), Waters et al. 2014 examined the association between attentional bias assessed in the field (using a PDA) and craving assessed in the field. Stated briefly, there was a significant between-subject correlation between attentional bias and craving.

EXPERIMENTAL STUDIES

Lab Studies Examining Effect of Attentional Bias Modification on Craving (Box 3)

Laboratory studies have examined the relationship between attentional bias modification (ABM) and craving. These studies have utilized several different attention retraining procedures designed to alter one's tendency to attend to, or avoid, salient cues

in the environment. In many studies, ABM has successfully changed attentional bias in the expected direction. One can also examine whether ABM changes craving. If ABM does change craving, and the effect of ABM on craving is mediated through changes in attentional bias, then this would provide strong evidence that attentional bias causes craving. Pertinent studies are summarized in Table 3.

In a study of current smokers, participants were divided into “attend” and “avoid” groups (Attwood, O'Sullivan, Leonards, Mackintosh, & Munafo, 2008). By completing visual probe tasks where the dot replaced either the smoking picture or neutral picture, significant changes in attentional bias were observed. Following cue exposure, there was also a significant difference in reported craving elicited from the avoid group compared to the attend group that was observed in male participants (Attwood et al., 2008). This is an important study as it was the first to use attention retraining tasks to manipulate attention bias for smoking-related cues. This finding indicates potential clinical utility in manipulating attention bias in order to reduce craving, which in turn may reduce smoking (Attwood et al., 2008).

In a study utilizing a similar design, participants were instructed to abstain from cigarettes for one hour prior to their lab appointment (Field, Duka, Tyler, & Schoenmakers, 2009). This study reported that smokers exhibited a significant bias at baseline whereby smokers responded more quickly on the visual probe task on probes that replaced smoking-related items compared to neutral items. Participants were randomly assigned to one of three retraining conditions: attend, avoid, and control (Field, Duka, et al., 2009). The attentional retraining tasks significantly increased attentional bias in the attend group and there was a near-significant reduction in

attentional bias in the avoid group (Field, Duka, et al., 2009). However, changes in attentional bias as a result of retraining did not persist when reassessed the next day indicating the effects of retraining may be short-lived. In addition, and most important for the current purposes, there was no effect of ABM on craving.

In a study involving smokers interested in quitting, participants completed multiple sessions of retraining tasks occurring before and after quit day (Begh et al., 2015). Compared to the procedure employed by Attwood et al. (2008), the participants in the retraining condition completed the VP task on more occasions, but each iteration was composed of fewer trials per task. The results from this study showed there was no significant attentional bias present at baseline. In addition, attention retraining did not result in changes in attentional bias, and there were no significant changes in craving as a result of retraining (Begh et al., 2015). The findings of this study indicate the relationship between attentional bias and craving as well as the relationship between attentional bias and smoking behavior may be weak or else the procedures utilized were not sensitive enough to capture the relationship (Begh et al., 2015).

Other researchers examined the efficacy of a single session attention retraining tasks in a study of 64 non-treatment seeking participants. Participants were randomly assigned to either the active training or control training condition and completed one session of the visual probe task (McHugh, Murray, Hearon, Calkins, & Otto, 2010). The participants in this study did not exhibit an attentional bias to smoking cues at baseline and the resulting reduction in attentional bias observed in the control group was not significant (McHugh et al., 2010). The results did not support the researchers' hypothesis that one training session was sufficient to significantly reduce bias. In light of the

findings, the researchers considered the possibility that the “dose” of training was insufficient to result in a significant change of attentional bias (McHugh et al., 2010).

In a recent study examining dose-response effects and the long-term utility of an attention retraining task, participants interested in smoking were randomly assigned to one of three conditions based on “dose amount” (Lopes, Pires, & Bizarro, 2014). This study used multiple “doses” of delivering attention retraining and showed they are capable of producing short-term changes in attention bias. This study also demonstrated a dose-response relationship to attention retraining where more sessions of retraining produced larger changes in bias (Lopes et al., 2014). Compared to other studies of attention retraining, data collected at long-term follow-up (6 months) supported the hypothesis that greater quantity of retraining sessions were capable of producing a long-lasting and durable change in attention bias (Lopes et al., 2014). However, there was no effect on craving.

Field Studies Examining Effect of Attentional Bias Modification on Craving (Box 4)

Kerst and Waters (2014) studied the utility of delivering attention retraining tasks on PDAs in participants’ natural environments. This study consisted of 60 non-treatment seeking smokers randomly assigned to either the active or control conditions of an attention retraining task (Kerst & Waters, 2014). The results of this study indicate the visual probe task is capable of reducing attentional bias when delivered on a PDA in the participant’s natural environment. This effect took approximately four days to occur. The study also found a significant reduction of craving after “compound” cue exposure (exposure to a stimulus containing smoking and neutral cues) in the active condition. This finding supported the hypothesis that attention retraining would result in attending away

from the smoking cue and towards the neutral cue, thereby leading to reduced craving in response to a cue (Kerst & Waters, 2014).

Lab Studies Examining the Effect of Craving on Attentional Bias (Box 5)

Three approaches could potentially be taken to manipulate craving as an independent variable. First, craving can be increased by increasing the “availability” of smoking (opportunity to smoke) (Wertz & Sayette, 2001). Second, craving is increased when smokers are required to abstain from smoking for an extended period of time (e.g. 12 or more hours) (Leventhal et al., 2010). Third, as noted earlier, craving is reliably increased after exposure to smoking (vs neutral) cues.

An effect of any of these three manipulations on attentional bias would be consistent with the idea that craving causes attentional bias. However, each manipulation is likely not a “pure” manipulation of craving. For example, as noted earlier, abstinence from smoking also impacts mood (as well as craving), and so any effect of deprivation could be due to mood. However, for each of the manipulations it is possible to examine whether the effect of the manipulation on attentional bias was mediated by craving. This would provide strong evidence that craving causes attentional bias.

Researchers have investigated how prior information about smoking opportunity or availability influences attentional bias to smoking-related cues (Wertz & Sayette, 2001). This study was based on previous addiction research that found significant differences in urge based on information outlined drug use opportunity. Participants were assigned to one of three groups where one group was informed they could smoke at the laboratory session (“Yes” group), one group was told they could not smoke (“No” group) and one group was told they might be able to smoke (“Maybe” group) (Wertz & Sayette,

2001). As expected, reported urge was highest in the “Yes” group followed by the “Maybe” group and then the “No” group. Most importantly, participants in the “Yes” group demonstrated the greatest attentional bias on the Stroop task followed by the “No” group, and the “Maybe” group (Wertz & Sayette, 2001). However, the correlation between reported urge and attentional bias was non-significant. Overall, this study provides only mixed support for the hypothesis that manipulating craving via smoking opportunity information causes changes in attentional bias (Wertz & Sayette, 2001).

As noted above, researchers have also manipulated deprivation level as a means of increasing urge to smoke (Mogg & Bradley, 2002). Participants completed the cognitive and self-report measures on two occasions: once after abstaining from cigarettes and once after smoking normally. Results indicated that overall, participants were slower to color-name smoking words on the smoking Stroop task and they responded more quickly to smoking cues in the VP task (Mogg & Bradley, 2002). In other words, smokers exhibited significant attentional bias on both measures. However, the deprivation state had no effect on attentional bias in either task, even though - as noted above - self-reported urge was correlated with attentional bias in each state. The authors concluded that attentional bias was more closely related to level of reported urge/wanting rather than level of deprivation (Mogg & Bradley, 2002).

Field et al. (2004) examined the effect of abstinence on attentional bias assessed using eye movements. They found that abstinence from smoking increased gaze duration on smoking stimuli (vs. neutral stimuli). That is, abstinence from smoking increased attentional bias to smoking cues, as assessed by eye movements. However, abstinence

from smoking did not have a significant effect on reaction time measures of attentional bias on the VP task.

In another lab study, participants completed two lab visits that were counterbalanced between participants. Participants were instructed to either remain abstinent for 10 hours prior to the session or were instructed to smoke as normal (Field, Munafo, et al., 2009). Similar to the study above, participants reported significantly greater levels of craving while in the deprived state compared to when they were instructed to smoke as normal. Overall, participants demonstrated a tendency to gaze longer at smoking cues and respond more quickly to probes that replaced smoking cues on the VP task revealing an attentional bias to smoking cues (Field, Munafo, et al., 2009). However, attentional bias was not moderated by deprivation status (Field, Munafo, et al., 2009).

In a large sample ($N=203$), Leventhal and colleagues (2010) assessed the effects of acute tobacco abstinence on subjective, cognitive, and physiological factors. Participants attended lab sessions before which they were instructed to either smoke as normal or abstain for at least 12-hours (Leventhal et al., 2010). As expected, the data indicated there was a large increase in craving in the abstinent condition compared to the ad libitum condition (Leventhal et al., 2010). The effect of abstinence on attentional bias as measured by the visual probe and smoking Stroop tasks was not significant on the primary outcomes, although there was evidence of an effect on secondary outcomes. There was, in addition, a clear and large effect of abstinence on self-reported attentional bias assessed by the SABQ. That is, smokers report that their attention is more easily

drawn to smoking stimuli when they are abstaining from smoking (Leventhal et al., 2010).

In a single-blind study manipulating deprivation, smokers were randomly assigned to either smoke as normal or to abstain for 12 hours prior to the lab session (Freeman, Morgan, Beesley, & Curran, 2012). The study also included a control group of individuals who were non-smokers. In this study, results indicated that abstinent smokers exhibited an attentional bias towards smoking cues. This finding was not significant in the satiated and non-smoker groups (Freeman et al., 2012). Individuals in the abstaining group also assigned greater intrinsic value to the smoking cues compared to the satiated and non-smoker participants (Freeman et al., 2012).

In a study examining the influence of cue exposure (smoking vs. neutral cues) on cognition, participants were instructed to abstain from smoking for one hour prior to lab visits to standardize the withdrawal effects across all participants (Field, Rush, Cole, & Goudie, 2007). Performance on the smoking Stroop task was compared after exposure to the neutral and smoking cue conditions. In the neutral conditions, participants were instructed to hold a pen for 10 seconds and in the smoking cue conditions they were instructed to hold a lit cigarette for 10 seconds. As expected, craving was significantly increased after smoking cue exposure. In addition, the smoking Stroop effect was increased following exposure to a smoking cue, indicating environmental stimuli can impact both craving and cognition (Field et al., 2007).

Field Studies Examining the Effect of Craving on Cognition (Box 6)

To date, to the best of the author's knowledge, there have been no field studies assessing changes in attentional bias as a result of manipulating, availability, deprivation, or cue exposure in the field.

Summary of Literature on Attentional Bias and Craving

Overall, both theory and data suggest that there is an association between attentional bias and craving. However, the data are somewhat unclear regarding the direction of any causal relationships. There is mixed evidence from experimental studies on whether ABM can reduce craving. In particular, no studies have reported an effect of ABM on general levels of craving. However, two studies did report an effect on a measure of cue-provoked craving in the expected direction (Attwood et al., 2008; Kerst & Waters, 2014). Similarly, there is mixed evidence from experimental studies regarding whether craving causes increases in attentional bias. A number of studies did find an effect of a craving-inducing manipulation on attentional bias (Field, Mogg, & Bradley, 2004; Field et al., 2007; Wertz & Sayette, 2001), but results have been inconsistent over measures. In addition, the author is not aware of any studies that have demonstrated that an effect of the craving-inducing manipulation on attentional bias was mediated by craving.

Overall, there appears to be an association between attentional bias and craving, but the direction of causal relationships, if any, remains unclear. The current study will address this general issue using EMA methodology.

Neurobiology of Attentional Bias and Craving

A few studies have examined the brain mechanisms underlying attentional bias in smokers and its association with craving. Brain imaging technology has been used to

examine the neurobiological processes underlying attentional bias to smoking cues and associations with craving. In one study, a group of smokers and a group of age- and gender-matched non-smokers participated in an fMRI study where brain scans were conducted while participants completed an attentional bias task, a line counting task while either neutral or smoking cues were presented (Luijten et al., 2011). The results of this study were that the dorsal anterior cingulate cortex, the superior parietal gyrus, and the superior temporal gyrus were activated in smokers compared to non-smokers when smoking cues were present in the line counting task. Subjective craving was also found to be correlated with activation in the insula and putamen (Luijten et al., 2011).

Another study examined brain processes underlying cue-induced craving in a virtual environment (Lee, Lim, Wiederhold, & Graham, 2005). The study reported increased activation in the prefrontal cortex, anterior cingulate cortex, inferior temporal cortex, and occipital lobe when participants were presented with smoking cues (Lee et al., 2005). Other researchers reported increases in the ventrolateral prefrontal cortex, ventromedial prefrontal cortex, and rostral anterior cingulate cortex during an attentional bias task (Goudriaan, de Ruiter, van den Brink, Oosterlaan, & Veltman, 2010). In sum, brain imaging studies have documented several brain regions, including the anterior cingulate cortex and parts of the prefrontal cortex, that appear to be involved in attentional bias and/or craving.

Most pertinent to the current study, researchers used the smoking Stroop task to identify which regions of the brain were activated when viewing smoking stimuli compared to neutral stimuli (Janes, Pizzagalli, Richardt, Frederick, Holmes, et al., 2010). This study demonstrated that attentional bias towards smoking cues was related to

increased brain activity in regions responsible for memory, emotion, interoception, and visual spatial processing. Attentional bias was also positively correlated with greater insula and amygdala reactivity (Janes, Pizzagalli, Richardt, Frederick, Holmes, et al., 2010). The insula and amygdala are thought to be involved in the assignment of salience to environmental stimuli and may be involved in the mechanism by which incentive salience is assigned to smoking cues, as described in IST 93.

An independent line of research in cognitive neuropsychology has reported that the insula is involved with subjective cue-induced urges and decision making (Naqvi, Rudrauf, Damasio, & Bechara, 2007). Naqvi et al. (2007) investigated whether damage or lesions to the insula were associated with “disruptions in smoking addiction”. According to Navqi et al. (2007), individuals were classified as having had a disruption of smoking addiction “if they fulfilled all four of the following criteria: (i) reporting quitting smoking less than 1 day after lesion onset, (ii) reporting that they did not start smoking again after they quit, (iii) rating the difficulty of quitting as less than three on a scale of one to seven, and (iv) reporting feeling no urges to smoke since quitting” (p. 532). Lesions to the insula were significantly associated with increases disruption in smoking addiction (compared to non-insula lesions). Moreover, right insula damage (compared to left insula damage) was associated with much higher rate of disruption in smoking addiction (OR= 10.87) (Naqvi et al., 2007). In another study of participants who experienced ischemic strokes, those with damage to the insula (vs. other brain regions) reported a significantly greater reduction in urge immediately following the stroke that was maintained at three-month follow-up (Abdolahi et al., 2017). However, both groups experienced an overall reduction in urge which indicates that other brain regions, in

addition to the insula, may play a role in the experience of urge during periods of withdrawal (Abdollahi et al., 2017).

In sum, relatively few studies have examined the brain mechanisms underlying attentional bias in smokers and its association with craving. The limited research suggests that insula activation may be implicated in both attentional bias to smoking cues and cue-induced craving, but more research is required to fully describe these linkages.

Attentional Bias and Relapse

As described above, the focus of this dissertation is on the association between attentional bias and temptation/craving, rather than the association between attentional bias and use/relapse. Nonetheless, this next section briefly reviews some literature on the association between attentional bias and use/relapse.

Attentional bias has been studied as a predictor of subsequent substance use or relapse for many drugs including heroin, cocaine, alcohol, and methamphetamine. For example, attentional bias assessed using the heroin Stroop task has also been shown to be a significant predictor of relapse status at 3-months among 110 heroin users attempting to maintain abstinence (Marissen et al.). This association persisted when controlling for subjective craving, suggesting that the association was not mediated by craving. A similar association was observed in a study involving 45 cocaine users attempting to maintain abstinence. Attentional bias assessed pre-treatment was positively associated with less treatment engagement and more positive drug tests post-treatment (Carpenter, Schreiber, Church, & McDowell, 2006). In a study involving 158 individuals who drank alcohol excessively, attentional bias was significantly correlated with long-term reduction in total number of drinking days, such that higher levels of attentional bias to alcohol cues

predicted less long-term reduction in drinking days (Cox, Pothos, & Hosier, 2007).

Attentional bias was also shown to be a significant predictor of treatment retention and relapse rates post-treatment for individuals addicted to methamphetamine (Hester, Lee, Pennay, Nielsen, & Ferris, 2010).

Most pertinent to the current dissertation are those studies that have examined the association between attentional bias to smoking cues and relapse during smoking cessation. As noted earlier, Waters et al. (2003) administered a smoking Stroop test containing smoking related and neutral words to examine attentional bias to 123 smokers attempting to quit. Participants were assessed on the first day of a quit attempt. Participants who exhibited more attentional bias were more likely to relapse in the short-term (first week) compared to those who exhibited less attentional bias. While this relationship is correlational, Waters et al. (2003) described several mechanisms through which a causal relationship between attentional bias and smoking/relapse may occur. For example, greater attentional bias may increase the potency and availability of smoking cues in the environment leading to craving and lapse (Waters, Shiffman, Sayette, et al., 2003).

Similar results were found in other studies of cigarette smokers undergoing a cessation attempt. Attentional bias assessed using the smoking Stroop task was significantly associated with relapse status 1-week following a cessation attempt (Powell, Dawkins, West, Powell, & Pickering, 2010). In another study, attentional bias measured using a smoking Stroop task predicted relapse after initial abstinence (Janes, Pizzagalli, Richardt, Frederick, Chuzi, et al., 2010). However, Waters, Shiffman, Mogg, & Bradley

(2003) reported that attentional bias assessed using the dot probe task was not associated with subsequent relapse.

Taken together, these findings lend support to further investigation of the role of attentional bias in developing and maintaining addiction and undermining cessation attempts. For example, attentional bias assessed pre-treatment might be used (in conjunction with other measures) to predict those individuals who may be at the highest risk of relapse. If the relationship between attentional bias and relapse is causal, interventions that reduce attentional bias could be useful as standalone or adjunctive treatments for smoking cessation.

CHAPTER 5: STUDY RATIONALE & SPECIFIC AIMS

PRELIMINARY STUDIES

Three preliminary studies are particularly pertinent to this dissertation study. First, Lammers (2017) examined the relationship between stress/negative affect and temptation episodes. Stress and negative affect (NA) were monitored by participants ($N=120$) during the first week of a cessation attempt at random times up to four times per day (random assessments; RAs), and at temptation episodes (TAs). Participants reported higher levels of craving at TAs (vs. RAs) (Figure 3), and higher levels of stress/negative affect at TAs (vs. RAs). Moreover, in the two hours prior to a temptation, stress/negative affect were elevated (see Figure 4). The data are consistent with the idea that stress/NA may provoke temptations during a quit attempt. Overall, the data demonstrate that the methodology used in the current dissertation was sufficiently sensitive to be able to detect significant elevations in a self-report measure in the hours before temptation episodes (Lammers, 2017).

The second preliminary study that is pertinent to the current study examined attentional bias, assessed with the drug Stroop task, before temptation episodes in heroin and cocaine dependent participants undergoing inpatient detoxification (Waters, Marhe, & Franken, 2012). The authors reported that attentional bias was higher at RAs assessed prior to a TA than at RAs more distal to TAs (Figure 5). The same was not true for implicit attitudes to drugs assessed by an Implicit Association Test. Overall, this study provides evidence that elevated attentional bias may precede temptations (and therefore provoke temptations), at least in heroin and cocaine addiction.

The third preliminary study of particular relevance to the current study is a study investigating craving and cognition during a cessation attempt (Waters et al., 2014). The

goal of the Waters et al. (2014) study was to examine associations between attentional bias, as assessed with the Smoking Stroop task on the PDA, and craving (assessed on a 1-7 scale) and self-reported attentional bias (assessed on a 1-7 scale) (Waters et al., 2014). (In the Waters et al. analysis, all observations were included in analyses, and attentional bias at TAs was not compared to attentional bias at RAs).

The main results of the Waters et al. (2014) study are as follows. First, participants exhibited significant attention bias, assessed with the smoking Stroop task, in the first week of a quit attempt. Second, attentional bias assessed with the smoking Stroop task was significantly associated with craving in a between-subject analysis (Waters et al., 2014). That is, participants who exhibited generally higher levels of attentional bias reported generally higher craving. Third, attentional bias assessed with the smoking Stroop task was significantly associated with self-reported attentional bias in a between-subject analysis (Waters et al., 2014). That is, participants who exhibited generally higher levels of attentional bias reported generally higher self-reported attentional bias. This finding bolsters the rationale for using self-reported attentional bias as a dependent variable in the proposed study. These analyses demonstrate that attentional bias, assessed in the field using the smoking Stroop task, is associated with self-reported craving and attentional bias.

SMOKING CESSATION: IMPORTANCE OF FIRST WEEK

As noted by Lammers (2017), most individuals who seek treatment for smoking cessation relapse very rapidly, often within seven days of quitting (Garvey, Bliss, Hitchcock, Heinold, & Rosner, 1992; Hughes et al., 2004). In addition, the vast majority of self-quitters also relapse in the first few days of a quit attempt (Hughes et al., 2004).

The literature provides estimates for relapse rates that range from 50% (Garvey et al., 1992) to approximately 80% (Garvey et al., 1992) during the first week of a cessation attempt. Furthermore, early lapses during a quit attempt predicted relapse at a later timepoint (Kenford et al., 1994).

Moreover, for the average quitter, withdrawal symptoms and craving peak early in a quit attempt and subsequently decline over time (Alessi, Badger, & Higgins, 2004). Some studies have reported that withdrawal symptoms and craving are related to subsequent relapse (Piper et al., 2008). Moreover, in a community sample there is evidence that intact executive control predicts successful smoking cessation (Brega, Grigsby, Kookan, Hamman, & Baxter, 2008). One study reported that the ability to remain abstinent on the first day of a quit attempt predicted abstinence at six months (Westman, Behm, Simel, & Rose, 1997).

These findings show that it is important to assess psychological processes in the first week of smoking cessation when craving is often elevated and cognition may be affected. For this reason, this dissertation will focus on the association between attentional bias and craving during the first week of an attempt to quit smoking.

Justification for Focus on Temptations

Temptation episodes, rather than relapse (first lapse) episodes, were the main focus in the current study. The justification for this focus as follows. First, as described earlier, temptation episodes are theoretically and clinically significant in their own right. For example, as noted by Waters et al. (2012), there is overlap between the psychological processes that underlie temptation and lapse episodes. For example, negative affect is elevated just prior to both lapse and temptation episodes, when compared to negative

affect at random assessments (Shiffman, Paty, et al., 1996). In addition, characteristics of temptation episodes have been associated with subsequent relapse. In particular, Shiffman et al. (1997) reported that duration (though not frequency) was prospectively associated with relapse. In the same study, in lapsers the peak reported urge during temptations (a measure of temptation intensity) significantly increased in the four days before the first lapse.

Second, the focus on temptation episodes during an attempt to maintain abstinence allows direct comparison to results of Lammers (2017) and with previous lab studies that examined the association between attentional bias and craving. As noted elsewhere in this dissertation, Lammers (2017) examined whether stress/negative affect was elevated prior to temptation episodes as individuals were trying to maintain abstinence. In laboratory studies that have examined the association between attentional bias and craving (reviewed earlier), participants would generally have been required to maintain abstinence during the laboratory session, as attentional bias and craving were assessed, and smoking behavior/relapse was rarely used as an outcome variable in these studies.

Third, several methodological challenges diminished enthusiasm for examining the association between attentional bias and specific relapse episodes during the first week of cessation. First, a review of the data indicated that a relatively low number of first relapse episodes were entered by participants, perhaps due to participant non-compliance with study procedures. Second, with the EMA protocol used there was difficulty verifying the specific time of relapse, so that the precise time of relapse was often not known with certainty. Nonetheless, exploratory analyses will examine

associations between relapse status at end of treatment and attentional bias. Specifically, as noted later the pattern of data of individuals who were abstinent at Week +4 (end of treatment) will be compared with those who were smoking at that time.

Temptation Episodes and Craving

As noted earlier, the current study will examine attentional bias before, during, and after temptation episodes. In addition, given the overlap between temptations and craving, and the importance of craving in Franken's (2003) model, the association between attentional bias and craving will also be examined in exploratory analyses.

STUDY RATIONALE

Overall, there is evidence that attentional bias is associated with craving in both laboratory and real-world settings. There is also evidence that temptation episodes are associated with higher levels of craving than non-temptation episodes (random assessments) (Figure 3). However, as noted earlier, there are sparse data on the relationships between attentional bias and temptations in a real-world context with cigarette smokers. In particular, the author is not aware of any data on the timeline of attentional bias before and after temptation assessments while individuals attempt to quit smoking. The current study examined whether attentional bias is elevated prior to, during, and after a temptation during the first week of a quit attempt. The first week was selected because many smokers would be expected to experience intense cravings and temptations to smoke during this period.

SPECIFIC AIMS

Specific Aim 1

To examine the relationship between attentional bias & Assessment Type during attempted abstinence from smoking.

Hypothesis 1: It is hypothesized that attentional bias will be higher at TAs vs. RAs.

Specific Aim 2

To examine whether attentional bias provokes temptations during attempted abstinence from smoking.

Hypothesis 2: It is hypothesized that attentional bias will be higher at RAs in the hours before TAs than at RAs distal from TAs.

Specific Aim 3

To examine whether temptations provoke attentional bias during attempted abstinence from smoking.

Hypothesis 3: It is hypothesized that attentional bias will be higher at RAs in the hours after TAs than at RAs distal from TAs.

In addition, a number of exploratory analyses were conducted, which are described in more detail later. Briefly, exploratory analyses examined associations between attentional bias and craving, relapse status, and race.

CHAPTER 6: METHODS

PARTICIPANTS

One hundred and nineteen adult cigarette smokers were recruited from the Houston, Texas, and Washington, DC, metropolitan areas. Participants volunteered to participate in a 1-week EMA study during a smoking cessation attempt. The 119 participants were a subset of 268 participants who enrolled in a “parent” smoking cessation study. Of the 268 participants, the final 231 participants were offered the opportunity to enroll in the EMA study, 129 volunteered to enroll, 119 provided EMA data that included data from the Stroop task, and 105 provided data from at least one day of abstinence (See Figure 6 for the Consort-type diagram). There were no significant differences in demographic variables between those participants who volunteered for the EMA study compared to those who did not volunteer. Participants all received the same smoking cessation intervention, as described below. The study was approved by the Institutional Review Board of the University of Texas M. D. Anderson Cancer Center and the Institutional Review Board of the Uniformed Services University of the Health Sciences.

As described by Lammers (2017), the inclusion criteria were: being between 18-65 years of age; smoking 10+ cigarettes per day for the past year; reporting being motivated to quit smoking within the next four weeks; having a home address and a functioning home telephone number; being able to speak, read, and write in English at an eight-grade literacy level; and reporting that English is the first language. Exclusion criteria were: evidence of active substance abuse or dependence; reporting regular use of tobacco products other than cigarettes; reporting use of nicotine replacement products or other smoking cessation medications (varenicline, bupropion); presence of another

household member enrolled in the study; self-reporting color-blindness; having an expired breath carbon monoxide (CO) < 10 ppm; being pregnant or breast feeding; and providing evidence of current suicidal ideation or depression.

The 119 participants (43% female) had an average age of 43.3 years ($SD = 11.1$), and they reported smoking an average of 19.1 ($SD = 7.9$) cigarettes per day. On an item assessing race, 52.9% of participants self-identified as White, 39.5% self-identified as Black or African American, and 7.6% self-identified another category. Participants' average score on the FTND (Heatherton, Kozlowski, Frecker, & Fagerstrom, 1991) was 5.11 ($SD = 2.07$). Their average expired level of CO in breath at orientation was 20.1 ppm ($SD = 8.66$), and the average level of cotinine (a nicotine metabolite) in saliva was 405.1 ng/ml ($SD = 242.0$).

In the parent study, for compensation participants received \$25 for completing the orientation session, and \$50 for completing each laboratory session (up to 5). The participants who enrolled in the EMA study also received \$2.50 for each RA that they completed; no compensation was received for completing temptation assessments.

PROCEDURE

Participants for the parent study were screened with a telephone interview during which they responded to question relating to smoking history and demographic information. Eligible participants were invited to attend an orientation session, during which they provided a sample of expired breath CO. The following assessments were also completed: the Rapid Estimate of Adult Literacy in Medicine (REALM; (Davis et al., 1991)); the Patient Health Questionnaire (PHQ; (Spitzer, Kroenke, & Williams, 1999)); Section K (Non-alcohol psychoactive substance use disorders) of the Mini

International Neuropsychiatric Interview (MINI; (Sheehan et al., 1998)); and the Alcohol Use Disorders Identification Test (AUDIT; (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993)).

Eligible participants attended up to five additional laboratory visits (see Figure 7), including two pre-quit laboratory visits, a quit day visit (Week 0), a visit one week post quit day (Week +1), and a visit at end of treatment (Week +4) four weeks after quit day. At the quit day visit (Week 0), participants were given the opportunity to volunteer to take part in the one-week EMA study. If a participant volunteered, he or she was trained how to use the PDA and completed an assessment on the PDA in the lab to ensure that they could use the device properly. Participants then took the PDA away with them and were instructed to complete up to four RAs administered daily on the PDA. RAs were programmed to occur at random times, 4 times per day. More specifically, based on the wake up and bed times on a given day (typically 8.00 AM and 11.00 PM respectively), the PDA program divided each day into 4 equal “periods”. Individual RAs were scheduled at a random time during each period.

As noted earlier, participants also completed participant-initiated assessments. As described by Lammers (2017), they self-initiated an assessment any time they experienced a temptation to smoke, defined as an occasion when they “felt an acute increase in the desire to smoke, or an occasion when they felt they came to the brink of smoking without actually smoking”. This assessment was initiated by pressing a button labelled “temptation or lapse assessment” on the PDA screen. Participants were also instructed to press this button if they lapsed (for the first time only), defined as “any smoking, even a puff”. Participants returned the PDA at Week +1.

TREATMENT

All participants received the same treatment. As part of the cessation study, participants were given a standardized self-help manual which used a standard relapse prevention/coping skills approach. Additionally, at each laboratory visit they also received brief (15-20 minute) individualized smoking cessation counseling from a licensed counselor using techniques from the Treating Tobacco Use and Dependence Clinical Practice Guideline (U.S. Department of Health and Human Services, 2008). Participants also received two brief telephone-counseling sessions at Week +2 and Week +3.

MEASURES

EMA Assessments

Self-Report Assessments

On PDA assessments (RAs and participant-initiated assessments), craving for cigarettes (“right now”) was assessed with a single item (“I am craving a cigarette”; 1-7 scale, 1=strongly disagree to 7=strongly agree). Self-reported attention to smoking was also assessed with a single item (“My attention is often drawn to cigarettes”; 1 = strongly disagree to 7 = strongly agree). As described in Lammers (2017), Stress (“right now”) was also assessed with a single item (“Right now”; “I am stressed”; 1=not stressed at all to 7=extremely stressed). Negative affect was assessed using seven items (relaxed, happy, enthusiastic, overall feeling, angry, sad, bored).

Recent smoking was assessed at each EMA assessment with two items. Participants indicated whether they had smoked that day (“Smoked so far today?”; Response options: “Yes” or “No”). The other item asked how much time had elapsed

since the last cigarette (“Time since last cigarette?”; Response options: “Just smoked/smoking now”, “5-30 minutes”, “31 minutes to 2 hrs”, “greater than 2 hours”).

Smoking Stroop Task

The smoking Stroop task was administered at every other assessment using methods described in Waters & Li (2008). At the alternate assessment, the Implicit Association Test (IAT) was administered, as described in (Waters, Miller, & Li, 2010). Data from the IAT are not reported in this dissertation.

For the smoking Stroop task participants were told that words written in blue, green, or red would be presented on the PDA screen, one after the other. The task was to identify as quickly and as accurately as possible the color the word was written in (Figure 8). The color identification task was made by pressing one of three response buttons on the PDA using a stylus. Participants were instructed that they could ignore the meaning of the word itself; the task was just to respond to the color. At each assessment, participants completed a practice block consisting of letter strings (e.g., MMMMMM) (33 trials), followed by two test blocks of 33 trials each. One test block consisted of neutral words and other block consisted of smoking words. There was a five second interval between the test blocks. Each word was presented in capital letters and remained on the screen until the participant responded or for 3 s (if the participant failed to respond).

The stimuli for the task involved 24 sequences of words (“lists”). Each list contained 11 smoking words, and 11 neutral words derived from the category “household objects” of comparable length and frequency to the smoking words (Waters & Li, 2008). Neutral words were: Sink, Iron, Sofa, Couch, Carpet, Lounge, Curtain, Hallway,

Bookcase, Tidy, Furniture. Smoking words were: Nicotine, Pack, Cigarette, Smoke, Inhale, Drag, Urge, Ashtray, Tobacco, Puff, Craving

At each assessment (RA or participant-initiated) a list was selected randomly (without replacement). The order of presentation of neutral and smoking words was counterbalanced over lists. That is, on 12 lists the neutral words preceded the smoking words, and on the other 12 lists the smoking words preceded the neutral words. Within each list, the order of presentation was determined using a random sequence.

On the Stroop task, reaction times (RTs) from incorrect responses were discarded, and so were RTs < 100 ms. To reduce the influence of RT outliers, median RTs for smoking words and for neutral words were computed for each block. For each assessment (RA or TA) the smoking Stroop effect was computed as the median RT on smoking words minus median RT on neutral words. Therefore, higher (more positive) smoking Stroop effects indicate greater attentional bias.

As reported in Waters et al. (2014), over all assessments from the 119 participants who provided data, the mean RT on neutral words was 808.3 ms ($SD = 162.8$), and the mean RT on smoking words was 826.3 ms ($SD = 170.1$).

After the Stroop task, an item asked the participant to indicate the number of occasions that he or she was interrupted while completing the Stroop task (e.g., by the telephone ringing or by somebody trying to talk to them; Response options: “No times”, “1 time”, “2 times”, “3 times”, “4+ times”).

Smoking Diary

Participants were instructed to make an entry in a smoking diary each night before going to bed indicating the number of cigarettes they had smoked on each day. They completed this diary throughout the parent study.

Relapse

To assess relapse at Week +4 (end of treatment), three types of data were used: self-reported smoking on the smoking diary, expired breath CO assessed in the laboratory, and levels of saliva in cotinine. Relapse at Week +4 was defined as “any smoking, even a puff, during the past 7 days”. To be coded as “abstinent” at Week +4, participants had to: 1) report smoking no cigarettes in the smoking diary in the week prior to Week +4; 2) provide an expired breath CO level ≤ 10 ppm at the Week +4 visit; and 3) have a salivary cotinine level ≤ 15 ng/ml at Week +4. Using these criteria, of the 105 participants who provided data from at least 1 day of abstinence during the EMA study, 22 (20.95%) were coded as abstinent at Week +4, and 83 (79.04%) were coded as relapsed.

Laboratory Assessments

Carbon Monoxide

CO levels in exhaled breath were assessed using a CO monitor (Vitalograph, Lexena, KS). CO was assessed at each lab session, including the quit-day and Week +1 visits. In the primary analysis, a breath CO level of ≤ 10 parts per million (ppm) was required to be considered abstinent at a given visit.

At each laboratory session, participants also reported the number of cigarettes they had smoked “so far that day”.

Salivary Cotinine

Salivary cotinine has been a common method for assessing nicotine exposure ("Biochemical verification of tobacco use and cessation," 2002; Ossip-Klein et al., 1986). Participants provided a saliva sample following instructions provided by Salimetrics LLC (State College, PA). Salivary cotinine levels were determined by Salimetrics using an enzyme immunoassay.

PDA Hardware and Software

The PDA used in the study was the HP iPAQ Pocket PC. Participants could press a "Suspend" button on the PDA to prevent it from presenting RAs for up to 2 hours. They could also press a "Delay" button at the time of RAs to delay RAs by 5 minutes (up to three times per RA). Participants could also alter the wake-up time and bed-time for each day at any point during the day. RAs were only presented between the designated wake-up and bed-times (i.e. RAs were not presented in the overnight hours).

DATA ANALYSIS

As noted earlier, 129 participants volunteered for the EMA study, and 119 provided data from the smoking Stroop task (Figure 6). Self-reported attentional bias was introduced into the study midstream, and data on this item were available from 108 participants (out of the 119 participants).

The primary analyses focused on assessments that occurred on days (which include "part days" in the case of the first and last day of EMA) on which there was no reported smoking. As described in Lammers (2017), a day during EMA was designated as an "abstinent day" if the participant, on all EMA assessments during that day: 1) endorsed "No" on the "Smoked so far today?" item on the PDA, and 2) endorsed "> 2

hours” on the “Time since last cigarette” item on the PDA. Additionally, data on quit-day were excluded if participants reported smoking “so far that day” at the quit-day visit. Data from the final EMA study day (the day of the Week +1 visit) was also excluded if participants reported smoking “so far that day” at the Week +1 visit. Similarly, data on quit day was excluded if CO level was > 10 ppm at the Quit Day, and data from the final EMA study day was excluded if CO level was > 10 ppm at the Week +1 visit. Using the above criteria, a total of 105 participants reported at least 1 day of abstinence, and these 105 participants completed in total 1306 RAs and 246 TAs during EMA.

Linear mixed models (LMM) were used for the primary analyses using SAS PROC MIXED. Primary analyses were also computed using SPSS MIXED which confirmed the results from the analyses using SAS. LMM analyses can deal with the dependence between observations due to clustering of data by participants. LMMs also permit different numbers of observations across participants, as is typical in EMA studies. For all models, a random (subject-specific) intercept and an autoregressive model of order 1 for the residuals within subjects (R matrix) was used. Day in study was included as a covariate in all models; for analysis of intensive longitudinal data Bolger and Laurenceau (2013, p. 71) have recommended including Time as a covariate.

In all models, attentional bias (smoking Stroop effect or self-reported attentional bias) was entered as the dependent variable. Separate analyses were conducted for the smoking Stroop effect and self-reported attentional bias. For the smoking Stroop effect, analyses were conducted when including all available data, and when subsetting to assessments in which participants reported no interruptions during task performance. In general, the two analyses revealed similar findings. To reduce the number of reported

analyses, analyses are reported for those subsetting to assessments with no reported interruptions. Parameter estimates were reported as an (unstandardized) measure of effect size (Wilkinson, 1999). All analyses used the Satterthwaite option for the denominator degrees of freedom (df=Satterthwaite in SAS PROC MIXED) which is the default option in SPSS. For all analyses alpha was set to .05 (2-tailed). For Specific Aims 1-3, *p* values < .10 were also noted.

The analytic plan for each hypothesis is described below (Appendix F also presents a visual depiction of comparisons involved in three Specific Aims).

Specific Aim 1

To examine the relationship between attentional bias & Assessment Type during attempted abstinence from smoking.

Hypothesis 1:

It is hypothesized that attentional bias will be higher at TAs vs. RAs.

For Hypothesis 1, the primary independent variable was Assessment Type (TA vs. RA). Assessment Type was treated as a random effect in the model (i.e., slopes were allowed to vary) if the *p*-value for the covariance parameter estimate (for Assessment Type) was less than .1 (Fitzmaurice, Laird, & Ware, 2011). Following Hedeker et al. (2009), a subject-level variable (level 2 variable) capturing the proportion of completed assessments that were TAs (i.e., no. of TAs divided by total number of assessments, a subject-level variable) was included in these models (in addition to Assessment Type). This means that the parameter estimate for Assessment Type provides the within-subject effect (i.e., that within subjects, attentional bias is higher at a TA than at an RA), which is the major focus of the current dissertation (Hedeker, Demirtas, & Mermelstein, 2009).

The proportion of completed assessments variable captures the between-subject association, i.e., whether subjects who reported a higher proportion of TAs exhibited generally greater attentional bias (Hedeker & Gibbons, 2006). As just noted, the current dissertation focuses on within-subject effects; to reduce the number of reported analyses (between-subjects effects are not reported).

Specific Aim 2

To examine whether attentional bias provokes temptations during attempted abstinence from smoking.

Hypothesis 2:

It is hypothesized that attentional bias will be higher at RAs that immediately precede TAs than at RAs distal from TAs.

For Hypothesis 2, following Lammers (2017), the primary independent variable was Time before TAs (a categorical variable), which was divided into three bins: RAs occurring within 2 hrs before a TA; RAs occurring 2-4 hrs before a TA; and RAs occurring more than 4 hrs before a TA (referred to as “Control RAs”). LMMs compared attentional bias for the following comparisons: RAs < 2 hrs vs. Control RAs; RAs 2-4 hours before a TA vs. Control RAs; RAs 0-4 hours before a TA vs. Control RAs. Note that Assessment Type was not included as an independent variable in this analysis, because all data were collected at RAs. Following Hedeker & Gibbons (2006), in each of the LMMs the model contained a subject-level term corresponding to the proportion of assessments that were proximal (within 4 hours, before the TA) of the TA for each subject. This ensures that the parameter estimate for Time (Time before TAs) provides the within-subject effect (i.e., that a subject’s attentional bias is higher at RAs proximal to

a TA than at distal “Control” RAs). Finally, it should be noted that for this Specific Aim (and Specific Aim 3) analyses compared data from proximal RAs to data from distal (Control) RA; data from proximal RAs were not compared with data from TAs. This is in part to reduce the number of analyses presented. In addition, it is not clear whether a difference is expected for this comparison (between proximal RAs and TAs), and the relatively small sample sizes would also reduce power for these analyses.

Specific Aim 3

To examine whether temptations provoke attentional bias during attempted abstinence from smoking.

Hypothesis 3:

It is hypothesized that attentional bias will be higher at RAs that immediately follow TAs than at RAs distal from TAs.

For Hypothesis 3, the primary independent variable was Time after TAs (a categorical variable), which was divided into three bins: RAs occurring within 2 hrs following a TA; RAs occurring 2-4 hrs following a TA; and RAs occurring more than 4 hrs following a TA (“Control RAs”). LMMs compared attentional bias for the following comparisons: RAs < 2 hrs vs. Control RAs; RAs 2-4 hours after a TA vs. Control RAs; RAs 0-4 hours after a TA vs. Control RAs. As for Specific Aim 2, Assessment Type was not included as an independent variable in this analysis (because all data derive from RAs). Again, in each of the LMMs the model contained a subject-level term corresponding to the proportion of assessments that were proximal (within 4 hours, after the TA) of the TA for each subject. This ensures that the parameter estimate for Time

(Time After TAs) provides the within-subject effect (i.e., that a subject's attentional bias is higher at RAs proximal to a TA than at distal "Control" RAs).

Exploratory Analysis

To make full use of the dataset, a number of exploratory analyses were conducted. Given the number of analyses, *p* values from these exploratory analyses should be treated with caution, but results may suggest hypotheses to be tested in future confirmatory studies.

First, analyses for Specific Aims 2 and 3 focused on comparing data on RAs from specific blocks of time (e.g., <2 hrs prior to TA, 2-4 hrs prior to TA, >4 hrs prior to TA). While this approach is consistent with previous analyses (e.g., Lammers, 2017), the author also explored using continuous measures of Time (for both Time before TAs and Time after TAs) to examine trends in attentional bias over time, both before and after TAs. Use of different "bin sizes" were also considered (e.g., breaking down data into 1-hr bins) but the small number of assessments occurring in the hours before and after a TA diminished enthusiasm for this approach.

Second, an exploratory analysis compared attentional bias at assessments with "maximal craving" (craving level of 7) against all other "non-maximal" assessments (craving levels 1-6). This analysis ignores Assessment Type (TA vs. RA). In this analysis, maximal craving is treated as the "episode" of interest (rather than TAs), and analyses will examine whether attentional bias is elevated prior to and after episodes of maximal craving. These analyses will use the same approach as those described for Specific Aims 1, 2, and 3 with the exception that Maximal Craving ("Maximal" vs "Non-Maximal") takes the place of Assessment Type (TA vs. RA). Therefore, the analyses will

examine 1) whether attentional bias is higher when craving is maximal (vs non-maximal), 2) whether attentional bias is higher in the hours before the occurrence of maximal craving, and 3) whether attentional bias is higher in the hours after the occurrence of maximal craving.

Third, an exploratory analysis compared attentional bias at assessments with “high craving” (defined as a craving level of 5-7) against all other “low craving” assessments (defined as craving levels 1-4). This analysis also ignores Assessment Type (TA vs. RA). In this analysis, “high craving”, as defined above, is treated as the “episode” of interest. These analyses will also use the same approach as those described for Specific Aims 1, 2, and 3 with the exception that High Craving (“high” vs “low”) takes the place of Assessment Type (TA vs. RA). Therefore, the analyses will examine 1) whether attentional bias is higher when craving is “high” (vs. “low”), 2) whether attentional bias is higher in the hours before the occurrence of “high craving”, and 3) whether attentional bias is higher in the hours after the occurrence of “high craving”.

Fourth, an alternative analytic strategy to examine prospective associations between attentional bias and temptations/craving is to conduct “lagged analyses” (Remmerswaal, Huijding, Bouwmeester, Brouwer, & Muris, 2014). These analyses can examine whether attentional bias at time t predict assessment type at the next assessment (time t_{+1}) when controlling for assessment type at time t . Conversely one can examine whether assessment type at time t predict attentional bias at the next assessment (time t_{+1}) when controlling for attentional bias at time t . Specifically, multilevel logistic regression analysis (PROC GLIMMIX in SAS) was used to examine whether attentional bias at time t predicts Assessment Type at time t_{+1} (including Assessment Type at time t and *Mean*

attentional bias as covariates). Multilevel linear regression analysis (PROC MIXED in SAS) was used to examine whether Assessment Type at time t predicts attentional bias at time $t+1$ (including attentional bias at time t , and proportion of TAs as covariates). Similar analyses were also used to examine the association between attentional bias and craving (assessed on a 1-7 scale). A limitation of lagged analyses is that for some assessments there will be long inter-assessment intervals. For example, one might consider that a temptation on Sunday evening may be unlikely to exert an influence on attentional bias on Monday morning. For this reason, lagged analyses were conducted sub-setting to assessments on which the assessment at time t and the assessment at time $t+1$ occurred on the same day.

Fifth, as noted earlier, exploratory analyses were conducted on the association between attentional bias and relapse status at Week +4. First, relapse status at Week +4 (Relapsed vs Abstinent) was included as an independent variable in analyses described for Specific Aim 1. This permitted an examination of whether relapsers have higher attentional bias at RAs or TAs (when abstinent). Second, as described in more detail later, the association between attentional bias and relapse status at Week +1 was also examined.

Last, exploratory analyses were conducted on the association between attentional bias and Race (coded as White, Black, or “Other”). Race was included as an independent variable in analyses. This permitted an examination of whether there are between-race differences in attentional bias at RAs or TAs (when abstinent).

Power Analysis

Field (2013) has written that it is not straightforward to compute power analyses for mixed models. Field (2013) referenced methods described in Twisk (2006), which use “traditional” methods (i.e., methods used on single-level data) and using an adjusted sample size that takes into account the correlated nature of the data. This approach was taken in this dissertation. Power analyses were computed using G*Power 3.1 (Faul, Erdfelder, Lang, & Buchner, 2007) and PASS version 12 (Hintze). Power analyses used $\alpha = .05$ and a 2-tailed test.

For Specific Aim 1 it was estimated a priori that participants will complete ~700 RAs and ~140 TAs with attentional bias data (smoking Stroop). It was also estimated that ~70 participants have completed at least 1 TA and at least 1 RA with attentional bias data. Using G*Power, for a paired-samples t-test. power = .80 to detect a Cohen’s d of 0.34 (which corresponds to a difference of 0.4 SD between the two conditions, assuming ρ , the correlation in the population, = .30), which is a small-to-medium effect size. However, given that each subject contributes multiple assessments for both RAs and TAs, this value (0.34) likely underestimates power. Using the repeated measures option in PASS, with the same parameters as above, power = .97 if each participant contributed two assessments in each condition (TA and RA). Under these condition, power = .80 to detect a Cohen’s d of 0.24. A more precise power estimate is difficult to compute because it depends on the average number of TAs and RAs completed (which will be very different across participants), as well as the degree of correlation between the conditions.

For Specific Aim 2, it was estimated that ~30 RAs will fall within 2 hrs before a TA, and there will be ~440 control RAs. Using G*Power, for a simple independent-samples t-test power = .80 to detect a Cohen’s d of 0.53 (a medium effect size). However,

this analysis likely substantially underestimates power because the data are likely correlated (i.e., many participants will contribute data at both timepoints). For Specific Aim 3, it was estimated that ~30 RAs will fall within 2 hrs after a TA, and there will be ~440 control RAs. Using G*Power, for a simple independent-samples t-test power = .80 to detect a Cohen's d of 0.53 (a medium effect size), but, again, this analysis likely substantially underestimates power because the data are likely correlated (i.e., many participants will contribute data at both timepoints).

CHAPTER 7: RESULTS

As noted earlier, of the 119 participants who completed at least 1 EMA assessment, 105 participants provided data on at least 1 day on which they reported abstinence. The 105 participants contributed data from 556 abstinent days, providing data on an average of 5.30 ($SD = 2.16$) days. During those 556 abstinent days, the 105 participants completed 246 TAs and 1306 RAs. As noted earlier, participants were scheduled to complete up to four RAs per day; the median compliance to complete RAs was 76.0% ($SD = 19.83$). On abstinent days, the median duration of EMA assessments that included the Stroop task was 4.38 minutes. The mean time of day for TAs (2.58 PM) did not differ from the mean time of day for RAs (3.19 PM), $F(1, 1446) = 1.53, p = .22$; 26.82% of assessments occurred before noon, 26.95% occurred between noon and 4.00 PM, 29.67% occurred between 4.00 PM and 8.00 PM, and 16.56% occurred after 8.00 PM.

Of those 105 participants, 19 (18.09%) were designated as abstinent at Week +1, and 22 (20.95%) were designated as abstinent at Week +4.

Number of TAs

On average, the 105 participants completed an average of 3.30 ($SD = 4.79$) TAs, and an average of 16.26 ($SD = 5.83$) RAs during the week (abstinent and non-abstinent days). Eighty-two participants (78.1% of the 105 participants) completed at least 1 TA. On abstinent days, the focus of the current study, the 105 participants completed an average of 2.34 ($SD = 4.36$) TAs, and 12.44 ($SD = 6.63$) RAs during the week. As noted earlier, self-reported attentional bias data were not available for all assessments. This was due to the fact that this assessment was added to the protocol midstream; of the 105

participants who provided data from at least 1 day of abstinence, self-reported attentional bias was collected from 94 participants. As noted earlier, the 105 participants provided data on the smoking Stroop task, but, this task was only administered at every other assessment. (The self-reported attentional bias assessment was administered at every EMA assessment).

Figure 9 shows that the number of reported TAs declined during the study period. Using a LMM, the number of TAs significantly declined over days, $F(1,1948) = 11.54$, $p = .0007$. These results include all days of data (abstinent and non-abstinent days) for the 105 participants, but similar results were obtained if only abstinent days were included in analyses.

Summary statistics on self-reported attentional bias and the smoking Stroop effect pertaining to primary and exploratory analyses are reported in Tables 4, 5 and 6 (see also Figures 10-12). Note that Figures 10-12 (and all other figures in the dissertation) present means and standard errors of assessment-level data (essentially ignoring the multilevel structure). Although easy to understand, subjects with larger numbers of assessments will be “overweighted” in these figures, and so the patterns should not be overinterpreted. Parameter estimates from LMMs, which do of course account for the multilevel structure, are presented in Tables 7, 8 and 9.

Specific Aim 1

Specific Aim 1 examined the relationship between attentional bias & Assessment Type during attempted abstinence from smoking. It was hypothesized that attentional bias would be higher at TAs vs. RAs.

As can be seen (Tables 4 and 7, Figure 10), self-reported attentional bias was significantly higher at TAs than RAs. The parameter estimate from the model (Table 7) indicated that self-reported attentional bias was 0.74 units higher (on a 1-7 scale) at TAs than RAs.

In contrast, the smoking Stroop effect did not differ by Assessment Type (Table 7, Figures 11 and 12).

In sum, Hypothesis 1 was only partially supported. Self-reported attentional bias was higher at TAs (vs. RAs), but there was no evidence that the smoking Stroop effect was higher at TAs (vs. RAs).

Specific Aim 2

Specific Aim 2 examined whether attentional bias provokes temptations during attempted abstinence from smoking. It was hypothesized that attentional bias would be higher at RAs that immediately precede TAs than at RAs distal from TAs.

As expected, the majority of RAs occurred more than four hours away from a TA with a much small number of RAs occurring within 2-4 hours and 0-2 hours of temptation assessments (Tables 4 and 7, Figures 10-12).

As shown in Table 7, there was little evidence that either self-reported attentional bias or the smoking Stroop effect was significantly elevated at RAs proximal to a TA (0-2 hours, 2-4 hours) compared to Control RAs distal to a TA. Self-reported attentional bias was 0.27 units higher at RA occurring within 4 hours of a TA (before a TA), but this difference did not reach significance ($p=.075$).

In sum, there was only weak support for Hypothesis 2. Self-reported attentional bias was marginally elevated in the hours prior to a TA, and there was no evidence that the smoking Stroop effect was elevated in the hours prior to a TA.

Specific Aim 3

Specific Aim 3 examined whether temptations provoke attentional bias during attempted abstinence from smoking. It was hypothesized that attentional bias would be higher at RAs that immediately follow TAs than at RAs distal from TAs.

As can be seen (Tables 4 and 7), self-reported attentional bias was not significantly different at RAs occurring 0-2 hours before TAs (compared to distal “Control” RAs) but was significantly different at RAs that occurred 2-4 hours after TAs and at RAs 0-4 hours after TAs (compared to distal “Control” RAs). According to the model, self-reported attentional bias was 0.48 units higher at proximal RAs occurring 0-4 hours after a TA (than at distal “Control” RAs). This provides evidence that self-reported attentional bias is elevated after TAs.

In contrast, when comparing proximal RAs with distal RAs, there was no evidence that the smoking Stroop effect is elevated after TAs. The smoking Stroop effect was significantly lower at RAs 0-4 hours after TAs (compared to distal “Control” RAs). This effect is in the opposite direction to that predicted. However, as indicated in Table 7, a significant effect was not found when considering each time period separately (0-2 hours, 2-4 hours).

In sum, there was mixed support for Hypothesis 3. Self-reported attentional bias was elevated in the hours after a TA, and there was no evidence that the smoking Stroop effect was elevated in the hours after a TA.

Exploratory Analyses

Analyses using a Continuous Measure of Time

Analyses for Specific Aims 2 and 3 focused on comparing data on RAs from specific blocks of time (e.g., <2 hrs prior to TA, 2-4 hrs prior to TA, >4 hrs prior to TA). While this approach is consistent with previous analyses (e.g., Lammers, 2017) and facilitates data visualization (Figures 10-12) it is also possible to conduct analyses using a continuous measure of Time (e.g., coded as “Hours before TA”). Exploratory analyses were conducted using a continuous measure of Time Before TA and Time After TA.

For RAs occurring within 8 hours prior to a TA, there was no evidence for a significant association between Time Before TAs (assessed in hours) and self-reported attentional bias, $n=183$ RAs, $PE = -0.09$, $SE = 0.06$, $p = .13$. The same was true when subsetting analyses to RAs occurring within 4 hours of a TA, $n=72$ RAs, $PE = 0.12$, $SE = 0.15$, $p = .43$. Similarly, for RAs occurring within 8 hours prior to a TA, there was no evidence for a significant association between Time Before TAs (assessed in hours) and the smoking Stroop effect, $n=72$ RAs, $PE = 4.03$, $SE = 6.46$, $p = .54$, and the same was true when subsetting analyses to RAs occurring within 4 hours of a TA, $n=44$ RAs, $PE = 1.64$, $SE = 19.95$, $p = .94$.

For RAs occurring within 8 hours after the occurrence of a TA, there was evidence for a significant association between Time After TAs (assessed in hours) and self-reported attentional bias, $n=122$ RAs, $PE = -0.16$, $SE = 0.07$, $p = .03$. That is, with each passing hour after a TA, self-reported attentional bias declined by 0.16 units. No significant association was observed when subsetting analyses to RAs occurring within 4 hours after an occurrence of a TA, $n=84$ RAs, $PE = 0.03$, $SE = 0.15$, $p = .85$. For RAs occurring within 8 hours after the occurrence of a TA, there was no evidence for a

significant association between Time After TAs (assessed in hours) and the smoking Stroop effect, $n=67$ RAs, $PE = 2.06$, $SE = 7.16$, $p = .78$, and the same was true when subsetting analyses to RAs occurring within 4 hours following a TA, $n=45$ RAs, $PE = 7.86$, $SE = 16.12$, $p = .58$.

Overall, these exploratory analyses yielded similar findings to those reported for Specific Aims 2 and 3. For self-reported attentional bias, there was evidence that self-reported attentional bias declined in the 8 hours following a TA, but there was no evidence that self-reported attentional bias increased in the 8 hours before a TA. In addition, for the smoking Stroop task there was no evidence that the smoking Stroop increased in the hours prior to a TA, nor was there evidence that the smoking Stroop effect declined in the hours following a TA.

Analyses of “Maximal” Levels of Craving

As noted earlier two additional analyses were examined. One compared attentional bias at assessments with “maximal craving” (craving level of 7) against all “non-maximal” assessments (craving levels 1-6). To restate, this analysis ignores type of assessment (TA vs. RA).

As can be seen (Tables 5 and 8, Figure 10), self-reported attentional bias was significantly different based on reported craving level (“maximal” vs “non-maximal”). Specifically, there were higher levels of self-reported attentional bias at assessments with reported craving of 7 (CR7) compared to assessments where reported craving was 1-6 (CR1-6). In contrast, no significant difference was found when examining the smoking Stroop effect as a function of reported craving (“maximal” vs “non-maximal”).

An additional analysis compared attentional bias prior to assessments with maximal craving (craving level of 7) against distal assessments (craving levels 1-6). As can be seen (Tables 5 and 8, Figures 10-12), neither self-reported attentional bias nor the smoking Stroop effect was significantly different at “non-maximal” craving assessments proximal to an assessment with “maximal craving” (0-4 hours) compared to “non-maximal” craving assessments distal to an assessment with maximal craving.

As noted earlier, an additional analysis compared attentional bias following assessments with maximal craving (craving level of 7) against distal assessments (craving levels 1-6). As can be seen (Tables 5 and 8, Figure 10), self-reported attentional bias was significantly higher at “non-maximal” assessments that occurred 0-4 hours after “maximal” assessments (compared to distal “Control” non-maximal assessments). However, a significant effect was not found when considering each time period separately (0-2 hours, 2-4 hours). The smoking Stroop effect did not differ significantly at proximal “non-maximal” craving assessments when compared to distal “Control” “non-maximal” craving assessments (Table 5 and Figures 11 and 12).

Analyses of “High” Levels of Craving

As noted earlier, an additional analysis compared attentional bias at assessments with “high” craving (craving levels 5-7) against all other assessments (craving levels 1-4). (As with the analysis of “maximal” craving, this analysis also ignores type of assessment (TA vs. RA)). As can be seen (Tables 6 and 9, Figure 10), self-reported attentional bias was significantly higher at “high” craving assessments (CR5-7) compared to “low” craving assessments (CR1-4). Again, there was no significant difference in the smoking Stroop effect as a function of craving (“high” vs. “low”).

A second additional analysis compared attentional bias prior to assessments with “high” craving (5-7) against distal assessments (craving levels 1-4). As can be seen (Tables 6 and 9, Figure 10), self-reported attentional bias was not significantly different between “low” craving assessments occurring less than 2 hours prior to a “high” craving assessments and distal “low” craving assessments. However, there was a significant difference when “low” craving assessments occurred 2-4 hours before a “high” craving assessment and when looking at “low” craving assessments occurring 0-4 hours before “high” craving assessments. In both instances, self-reported attentional bias was significantly higher at the proximal “low” craving assessments compared to the distal “low” craving assessments (i.e., those more than 4 hours distal from a “high” craving assessment).

The smoking Stroop effect did not differ as a function of the time (“proximal” vs “distal”) of the “low” craving assessment (Tables 6 and 9, Figures 11 and 12). It should be noted that the smoking Stroop effect was marginally higher ($p = .057$) at “low” craving assessments occurring within 4 hours of a “high” craving assessments than at distal “low” craving assessments.

Another additional analysis compared attentional bias following assessments with “high” craving (5-7) against distal assessments (craving levels 1-4). As can be seen (Tables 6 and 9, Figure 10), self-reported attentional bias was significantly higher than at distal “Control” assessments only when “low” craving assessments occurred 2-4 hours after “high” craving assessments.

The smoking Stroop effect did not differ significantly at proximal “low” craving assessments when compared to distal “Control” “low” craving assessments (Tables 6 and 9, Figures 11 and 12).

Lagged Analyses

As noted earlier, an alternative analytic strategy to examine prospective associations between attentional bias and craving is to conduct “lagged analyses”. These analyses can examine whether attentional bias at time t predict assessment type (TA vs RA) at the next assessment (time t_{+1}) when controlling for assessment type at time t . Conversely one can examine whether assessment type at time t predicts attentional bias at the next assessment (time t_{+1}) when controlling for attentional bias at time t .

Similarly, one can use lagged analyses to examine whether attentional bias at time t predicts craving (1-7 scale) at the next assessment (time t_{+1}) when controlling for craving at time t . Conversely one can examine whether craving at time t predicts attentional bias at the next assessment (time t_{+1}) when controlling for attentional bias at time t .

As noted earlier, lagged analyses used assessments for which the assessments at time t and time t_{+1} occurred on the same day. For lagged analyses, the median interval between assessments was 3.23 hours.

Results of LMMs are presented in Tables 10 and 11. Table 10 shows that Assessment Type (RA vs. TA) predicts self-reported attentional bias at the following assessment, providing some evidence that temptations provoke attentional bias. There was no evidence that self-reported attentional bias predicts the assessment type at the next assessment.

Table 11 shows that craving, assessed on a 1-7 scale (and ignoring Assessment Type), predicts self-reported attentional bias at the following assessment, providing some evidence that craving provokes attentional bias. In addition, self-reported attentional bias also predicts craving at the next assessment. These data (i.e., the data reported in Tables 10 and 11) provide the strongest evidence in the study for bidirectional relationships between self-reported attentional bias and craving.

For the above analyses, there was no evidence of any significant associations involving the smoking Stroop effect.

Attentional Bias as a function of Relapse

Overall, of the 105 participants who had available data from abstinent days, 22 were coded as abstinent at Week +4 (end of treatment), and 83 were coded as relapsed. Figure 13 shows self-reported attentional bias, and the smoking Stroop effect as a function of Relapse Group at Week +4 and Assessment Type (RA vs TA). As can be seen, self-reported attentional bias was higher in participants who were coded as relapsed at Week +4, $PE = -0.80$, $SE = 0.34$, $F(1, 87.5) = 5.45$, $p = .02$. As suggested by Figure 13, there was no evidence for a Relapse Group x Assessment Type interaction ($p = .44$). In sum, individuals who were coded as relapsed at the end of the study reported generally higher levels of attentional bias when abstinent during the first week of a quit attempt.

Figure 13 also shows the smoking Stroop effect as a function of Relapse Group at Week +4 and Assessment Type (RA vs TA). As can be seen, the smoking Stroop effect appears to be higher at TAs in participants coded as abstinent at Week +4, but not at RAs. However, the Relapse Group x Assessment Type interaction did not reach significance, $PE = 62.97$, $SE = 34.76$, $F(1, 48.6) = 3.28$, $p = .08$. Moreover, the between-group

(Relapsers vs. Abstainers) difference in the smoking Stroop effect at TAs also did not reach significance, $PE = 58.06$, $SE = 30.75$, $F(1, 37.8) = 3.57$, $p = .07$.

Some consideration was given to plotting a timeline of attentional bias before and after TAs, as a function of Relapse group. However, the dearth of assessments in the 4 hours before and after TA, particularly in Abstainers (the smaller group), diminished enthusiasm for these analyses. For example, in the 2 hours prior to a TA, data on self-reported attentional bias were available from 7 assessments from abstainers, and 34 assessments from relapsers. In the period 2-4 hours prior to a TA, data on self-reported attentional bias were available from 4 assessments from abstainers, and 27 assessments from relapsers. In the 2 hours following a TA, data on self-reported attentional bias were available from 9 assessments from abstainers, and 28 assessments from relapsers. In the period 2-4 hours following a TA, data on self-reported attentional bias were available from 7 assessments from abstainers, and 40 assessments from relapsers. Of course, there were even less data available from the smoking Stroop task (as it was administered at every other assessment). In sum, small sample sizes precluded examination of between-group differences in trajectories before and after TAs.

Relapse analyses were also conducted as described above using a CO cut-off of ≤ 4 ppm (rather than 10 ppm) as designating abstinence. That is, to be coded as abstinent, participants had to report no smoking during the previous 7 days, have a level of cotinine in saliva ≤ 15 ng/ml, and have an expired CO of ≤ 4 ppm. This did not alter findings, as all participants designated as abstinent at Week +4 had a CO ≤ 4 ppm (the highest level reported was 4 ppm).

Analyses were also conducted as a function of relapse status at Week +1. To be coded as abstinent at Week +1, participants had to report no smoking during the previous 7 days, have a level of cotinine in saliva ≤ 15 ng/ml, and have an expired CO of ≤ 10 ppm at the Week +1 visit. Overall, of the 105 participants who had available data from abstinent days, 19 were coded as abstinent at Week +1 and 86 were coded as relapsed. Figure 14 shows self-reported attentional bias, and the smoking Stroop effect, as a function of Week +1 Relapse Status and Assessment Type (RA vs TA). As can be seen, self-reported attentional bias appears to be higher in participants who were coded as relapsed at Week +1, but the main effect of Relapse Group was not significant, $PE = -0.22$, $SE = 0.36$, $F(1, 87.2) = 0.38$, $p = .54$, and neither was the Relapse Group x Assessment Type interaction ($p = .55$). As shown in Figure 14, the smoking Stroop effect appeared to be higher at TAs in participants who were designated as relapsed at Week +1, but not at RAs. The Relapse Group x Assessment Type interaction was significant, $PE = 72.46$, $SE = 35.63$, $F(1, 46.3) = 4.14$, $p = .04$, and the between-group (Relapsers vs. Abstainers) difference in the smoking Stroop effect at TAs was also significant, $PE = 76.56$, $SE = 31.38$, $F(1, 35.4) = 5.95$, $p = .02$.

In additional analyses, the analyses involving Relapse (a level 2 variable) described above were recomputed when including age, gender, and race (level 2 variables) as covariates. The significant results reported above (assuming $\alpha = .05$) were maintained when including these variables as covariates in the models.

Attentional Bias as a function of Race

Attentional bias was also examined as a function of Race. Overall, of the 105 participants who provided data from abstinent days, 55 (52.38%) self-reported as White,

43 (40.95%) self-reported as Black or African American, and 7 (6.67%) reported as Other. Figure 15 shows self-reported attentional bias, and the smoking Stroop effect as a function of Race. When self-reported attentional bias was the dependent variable, there was no main effect of Race, $F(2, 89.6) = 2.14, p = .12$, nor was there a Race x Assessment Type interaction, $F(2, 52.2) = 1.53, p = .23$. Similarly, when the smoking Stroop effect was the dependent variable, there was no main effect of Race on the smoking Stroop effect $F(2, 75.6) = 0.72, p = .49$, nor was there a Race x Assessment Type interaction, $F(2, 44.7) = 0.39, p = .68$.

CHAPTER 8: DISCUSSION

MAIN FINDINGS

The main findings of the study were as follows. First, with respect to Specific Aim 1, self-reported attentional bias was higher at TAs than RAs. However, contrary to hypothesis, there was no evidence that the smoking Stroop effect was higher at TAs than RAs. Second, regarding Specific Aim 2, there was only weak evidence that attentional bias is elevated in the hours before a temptation. Self-reported bias was only marginally significantly higher at proximal RAs than distal RAs in one analysis, and there was no evidence that the smoking Stroop effect was elevated in the hours before a temptation. Third, regarding Specific Aim 3, self-reported attentional bias was elevated at RAs occurring in the 4 hours after a TA. In sum, for self-reported attentional bias there was some support that attentional bias was elevated at TAs, and after a TA. For the smoking Stroop task, there was no evidence that the smoking Stroop effect was elevated before, during, or after a TA.

The study also included a number of exploratory analyses. Results from exploratory analyses are discussed in more detail later, but key findings are summarized here. First, there was evidence that self-reported attentional bias was elevated (compared to “Control” assessments) before “maximal” craving assessments as well as after “maximal” craving assessments, although the evidence was stronger for the latter. Second, there was evidence self-reported attentional bias was elevated before “high” craving assessments as well as after “high” craving assessments. There was little evidence that the smoking Stroop effect was elevated before, during, or after, “maximal” or “high” craving assessments. Third, self-reported attentional bias was significantly related to craving at the next assessment, and craving was significantly related to self-

report attentional bias at the next assessment. This result gives the strongest support in the study for a reciprocal relationship between self-reported attentional bias and craving. Again, there were no significant associations involving the smoking Stroop effect in these “lagged analyses”. Finally, there was evidence that self-reported attentional bias was generally higher in individuals who relapsed at the end of study, and the smoking Stroop effect was higher at TAs (but not RAs) in relapsers (compared to abstainers).

Specific Aim 1

Self-reported attentional bias, but not the smoking Stroop effect, was significantly higher at TA compared to RA, which partially supports Hypothesis 1. The finding of higher subjective attentional bias at temptations (compared to RAs) is consistent with theory (Franken, 2003). Other subjective reports are also higher at temptations (compared to RAs). For example, using the same dataset, Lammers (2017) reported that self-reported stress and negative affect (stress/negative affect) were higher at TAs than RAs. Taken together, these findings indicate that multiple subjective experiences are elevated during a temptation episode. Stated another way, attentional bias and stress/negative affect may increase the probability of reporting a temptation episode. It is not clear if reported attentional bias and stress/negative affect exert independent influences on propensity to report a temptation episode, or whether their influences interact such that reports to temptations are associated with particularly high levels of attentional bias and stress/negative affect. As described later, such questions may be further examined with the use of machine learning approaches.

In contrast, contrary to hypothesis, the smoking Stroop effect was not higher at TAs than RAs. At first sight, this result seems inconsistent with the findings of Waters et

al. (2014), who reported that attentional bias, assessed using the smoking Stroop, was associated with craving. However, the association reported by Waters et al. was a between-subject association, and the within-subject association (the focus of analyses in this dissertation) was not significant in Waters et al. (2014). That is, the analyses reported in Waters et al. (2014) revealed that individuals who reported generally high craving reported a generally high smoking Stroop effect. However, when an individual reported more craving than usual, attentional bias was not elevated, indicating that the within-subject association was not significant.

Moreover, the analysis presented in Waters et al. 2014 involved craving rather than assessment type (TA vs RA). However, in a sample of heroin-dependent participants (most of whom also used cocaine) undergoing detoxification, Waters et al. (2012) did report that attentional bias was higher at temptations than RAs (in a within-subject analysis). The reason for the different results across the two addictions (tobacco addiction vs. heroin addiction) is not clear. Speculatively, it is possible that attentional bias in heroin-dependent participants is elevated at TAs as participants are less able to use executive processes to control attention than smokers particularly during temptations (see Field and Cox, 2008, Fig. 1). Relatedly, a meta-analysis reported that attentional bias in opioid addiction is generally larger than attentional bias in tobacco addiction (MacLean, Sofuoglu, Brede, Robinson, & Waters, 2018).

One may wonder why the subjective measure of attentional bias was higher at temptations (compared to RAs), but the “objective” measure (smoking Stroop effect) was not. There are several explanations for this pattern of data. First, comparisons between the results for the two measure types (i.e., self-reported attentional bias and the smoking

Stroop effect) are complicated by the presence of method differences between these two measures. First, as noted earlier, the self-reported attentional bias measure was added after the start of the parent study and was only administered to a subset of participants who completed the smoking Stroop task. In addition, the smoking Stroop task was administered at every second assessment, whereas the self-reported attentional bias measure was administered at every assessment. This reduces the total number of times participants completed the smoking Stroop task compared to the self-report attentional bias measure (and total number who completed both measure types). For the smoking Stroop task, the lower number of assessments reduces power and increases the likelihood of committing a type II error. Thus, it is possible that the different pattern of data between the two measure types (i.e., self-report vs. smoking Stroop) reflect, at least in part, method differences.

In addition, it is also likely that self-reported attentional bias and the smoking Stroop task do not measure the same phenomenon. Although automatic attention capture assessed by the smoking Stroop might be expected to influence judgments of self-reported attentional bias (i.e., individuals who exhibit greater attentional bias on the smoking Stroop task may report greater attention capture by smoking cues), self-reported attentional bias relies on participants' memory to report attention capture smoking cues, and this could produce different data. Moreover, the smoking Stroop task assesses cognitive processes "at the moment" of assessment, whereas the self-report measure presumably assesses processes in the recent past. Other cognitive processes are likely involved in the self-report assessment, such as response biases, that would be expected to further weaken any association. Empirically, Waters et al. (2014) reported that there was

only a weak association between the smoking Stroop effect and self-reported attentional bias. Furthermore, it is also possible that attentional bias assessed by the smoking Stroop task might only be elevated in either the lead up to or aftermath of a temptation episode (and not during the temptation itself). Assessment of cognitive processes in the field may also have measurement error (though associations have been documented in other studies, as noted above). Overall, the cognitive processes assessed by the self-report measure may be more sensitive to the presence of a temptation than those assessed by the smoking Stroop task. Further research using larger samples is required to examine this further.

Specific Aim 2

As previously stated, there was only weak evidence that attentional bias is elevated in the hours before a temptation; the difference between self-reported attentional bias at proximal RAs (0-4 hours) compared to distal RAs was only marginally significant. Similar to the non-significant association in Specific Aim 1, there was no evidence that the smoking Stroop effect was elevated at proximal RAs compared to distal RAs.

The finding for the smoking Stroop effect is not consistent with findings reported by Waters et al. (2012), who reported that attentional bias was significantly elevated in the hours leading up to a temptation episode. However, there are some important differences between the current study and the study reported in Waters et al. (2012) that should be considered. Waters et al. (2012) found that the drug Stroop effect (heroin and cocaine Stroop effects) was significantly higher at RAs which occurred less than 1 hour before TAs (compared to distal RAs). The drug Stroop effect was not higher at RAs occurring 1-3 hours before a TA (compared to distal RAs). The current dissertation study was limited by the relatively small number of assessments occurring in the hours prior to

a TA and time groupings were set at 0-2 hours and 2-4 hours preceding a TA. Given the small number of assessments available in the current dissertation study, it was difficult to examine patterns hour-by-hour. It is possible the smoking Stroop effect is elevated in the minutes preceding an entry of a TA, but, again, the study was unable to examine this due to a shortage of assessments occurring in each time block. If true, it would take a large number of RAs occurring in the minutes and hours preceding a TA to determine exactly when attention bias changes.

Additionally, as noted above, attentional bias may differ between smokers and heroine/cocaine dependent individuals. Heroin users, compared to cigarette smokers, may exhibit a generally more robust attentional bias to drug cues (see MacLean et al., 2018), which may increase the likelihood of findings differences as a function of time.

It should be noted that although there was only weak evidence that attentional bias was elevated before a TA, Lammers (2017) reported significant elevation in stress and negative affect at RAs in the hours leading up to a temptation episode (compared to distal RAs). Therefore, the methods used in the current dissertation were able to detect changes in some psychological constructs prior to a TA. This may mean that any prospective association between stress/negative and temptations is stronger than that between attentional bias and temptations, but further research would be required to confirm this.

If stress/negative affect are elevated before a TA, as reported by Lammers (2017), one might wonder whether the elevation in stress/negative affect has any implications for attentional bias during that period. Easterbrook (1959) argued that high arousal stress/negative affect influences attentional focus such that increases in stress/negative

affect could potentially narrow attentional focus and reduce attentional bias. On the other hand, Robinson and Berridge (1993) argue that there is cross-sensitization between stress and the wanting system such that stress (in particular chronic stress) should increase wanting (and therefore attentional bias). There are also reports from laboratory studies that acute stress increases attentional bias to addiction-related cues, at least in drinkers (Field & Powell, 2007; Field & Quigley, 2009). Thus, it is not clear whether stress/negative affect is expected to increase or decrease attentional bias in smokers. This issue should be further investigated in smokers both in laboratory studies and EMA studies.

Specific Aim 3

Self-reported attentional bias was found to be elevated at RAs 0-4 hours after a TA (compared to distal RAs). However, there was no evidence that the smoking Stroop effect was elevated at RAs occurring in the hours after a TA. To the contrary, there was even evidence that it was *lower* 0-4 hours after a TA (i.e. opposite to prediction). Similar to results for Specific Aims 1 and 2, there is a difference in the pattern of results between self-reported attentional bias and attentional bias assessed by the smoking Stroop task. These differences lend additional support to the idea that the two measure types capture different phenomena.

As noted in the introduction, Franken's (2003) model assumes that attentional bias can cause craving, and that craving can cause attentional bias. Therefore, the elevation of self-reported attentional bias after a TA is consistent with this model. Franken did not describe in detail the mechanisms underlying the causal relationship between craving and attentional bias. One explanation for why self-reported attentional

bias increases after a temptation episode is related to the idea of “contingent capture.” Rather than only being the outgrowth of automatic processes, increases in attentional bias may be a result of voluntary or explicit efforts towards seeking out salient and rewarding stimuli in one’s environment. The experience of temptation episodes may cause smokers to voluntarily attend to smoking cues, which can increase attentional “pop out” of these cues (Folk et al., 1992; see also Kahneman 2011, p. 23).

Whatever the mechanisms linking temptations and attentional bias, the data may indicate that individuals are at greater risk for relapse both following a temptation episode because their attention is more readily captured by smoking cues. This would mean that cessation programs would need to consider that the hours after a temptation episode are also a “vulnerable period”.

EXPLORATORY ANALYSES

“Maximal” vs “Non-Maximal” Craving

As noted earlier, a number of exploratory analyses were conducted on the data. In the first exploratory analysis, assessments were classified as “maximal” craving assessments when participants reported craving of 7 and as “non-maximal” when participants reported craving of 1-6. Self-reported attentional bias, but not the smoking Stroop effect, was significantly higher at “maximal” assessments compared to “non-maximal” assessments which is consistent with other studies showing positive correlations between self-reported attentional bias and craving (Waters, Shiffman, Bradley, & Mogg, 2003; Waters et al., 2014). When compared to control “non-maximal” assessments, self-reported attentional bias was only elevated at “non-maximal” assessments when aggregated 0-4 hours after a “maximal” assessment. This finding is

similar to that reported for the analyses of assessment type and suggests that self-reported attentional bias is elevated after a report of elevated craving. Taken together with the data from specific Aim 3, it suggests that attentional bias is elevated after the report of temptation and/or after elevated craving.

“High” vs “Low” Craving

Similar to the previous exploratory analysis, assessments were grouped based on craving level with “high” craving assessments consisting of craving levels 5-7 and “low” craving assessments consisting of craving levels 1-4. Similar to above, self-reported attentional bias (but not the smoking Stroop effect) was significantly higher at “high” craving assessments compared to “low” craving assessments. However, there was more evidence that self-reported attentional bias was elevated prior to “high” craving assessments compared to after “maximal” craving assessments. That is, self-reported attentional bias was significantly higher at RAs 0-4 hours before a “high” craving assessments compared to distal (control) RAs. Self-reported attentional bias was also significantly higher 2-4 hours after “high” craving assessments.

Overall, these findings indicate self-reported bias is elevated prior to “high craving” and may be associated with subsequent changes in craving. However, only self-reported attentional bias produced significant results and the smoking Stroop effect was not found to be significantly associated with this measure of craving. The association between craving and attentional bias is further explored with the use of “lagged analyses” presented below.

Lagged Analyses

Lagged analyses were conducted to directly examine if prospective relationships existed between variables. While there was a significant association between assessment type and self-reported attentional bias at the subsequent assessment, there was no significant association from self-reported attentional bias to assessment type at the next assessment. There were no significant relationships between the smoking Stroop and assessment type. Thus, there was no evidence of a reciprocal relationship between attentional bias and temptations. The evidence for temptations preceding self-reported attentional bias was stronger than the evidence for self-reported attentional bias preceding temptations. These results seem to support the results of Specific Aims 2 and 3, in which the evidence that self-reported attentional bias was elevated following a TA is stronger than the evidence that self-reported attentional bias was elevated before a TA. The consistency in results across different analyses bolsters confidence in this finding.

In contrast to the above findings, analyses showed a significant reciprocal relationship between self-reported attentional bias and craving, when craving was assessed on a 1-7 scale. Self-reported attentional bias was significantly associated with craving at the subsequent assessment, and craving was associated with self-reported attentional bias at the subsequent assessment. These analyses provide the strongest evidence in the current dataset for a reciprocal (prospective) association between attentional bias and craving (and for Franken's (2003) model). This finding may have been easier to detect with these analyses because there is greater power to detect associations involving craving (compared to assessment type) because craving is assessed on a 1-7 scale (rather than a binary scale). Alternatively, craving (compared to

assessment type) may be more strongly associated with self-reported attentional bias. This issue is discussed later in more detail.

Ultimately, lagged analyses are useful in order to better understand how attentional bias, craving, and temptation are related to each other over time, and it may be possible to intervene in the sequence of events that lead to increased craving and temptations. Specific to the current study, it may be useful for interventions to target craving or attention bias (or both). This issue is addressed in the future directions sections.

Relapse Status

Attentional bias was examined as a function of relapse at two time points, Week +4 (end of treatment) and Week +1. As noted earlier, at Week +4, there was a main effect of Relapse group wherein relapsers exhibited higher self-reported attentional bias than non-relapsers. The absence of a Relapse group by Assessment Type interaction indicated that the effect of Relapse group did not differ on RAs and TAs. In contrast, for the smoking Stroop effect there were no significant effects involving Relapse group at Week +4 (although the Relapse group x Assessment Type interaction approached significance). However, at Week +1 the Relapse group x Assessment Type interaction did reach significance such that the Relapsers exhibited higher attentional bias at TAs (but not RAs) than abstainers. At Week +1 there was no effect of Relapse group on self-reported attentional bias.

To the best of the author's knowledge, the data at Week +4 reveal the first documented association between relapse status and self-reported attentional bias assessed using a single item. Robinson et al. (2015) reported an association between self-reported

attentional bias assessed using the 8-item Subjective Attentional Bias Questionnaire (SABQ) and relapse status at Week +4. This indicated that participants who reported higher scores on the SABQ were more likely to have relapsed at Week +4. (The sample in Robinson et al. (2015) was derived from the parent study of the current dissertation study.). The current study extends these findings by revealing that even a single item assessing attention capture is associated with relapse status. Methodologically this is important as administration of a single item during EMA is less burdensome for participants than multi-item assessments. In addition, although self-report measures cannot provide detailed information on the precise mechanisms of attentional bias, they may be useful as predictors in statistical and machine learning models that identify individuals at risk of relapse.

As was the case with other analyses presented in this dissertation, analyses conducted on the two dependent variables (i.e., self-reported attentional bias and smoking Stroop effect) yielded different results. For the smoking Stroop effect, the data suggested that relapsers had higher attentional bias at temptations than abstainers, but not at RAs. This result is the same as that reported by Marhe et al. (2013) in a group of opiate-dependent individuals undergoing detoxification. Marhe et al. reported that individuals who would subsequently relapse during the first week of detoxification had higher attentional bias at TAs (vs. those who did not relapse during the first week), and they also reported a significant Relapse group by Assessment Type interaction. What is puzzling about the results in this dissertation is that attentional bias in abstainers was low in absolute magnitude (rather than the attentional bias in relapsers being high in absolute magnitude) (see Figure 14). Stated another way, it appears that the smoking Stroop effect

was suppressed in abstainers (during TAs). This specific pattern of data was not anticipated. It is possible that abstainers during the first week are particularly good at dealing with attentional bias during temptations and utilize higher order strategic or compensatory processes to not only override the attentional bias (Field & Cox, 2008; Mathews & Sebastian, 1993) but to actually speed responding on the smoking words. Whatever the explanation, in common with Marhe et al., it appears that attentional bias at temptations is more closely associated with relapse status than attentional bias at RAs, at least when the smoking Stroop task is used. The current finding (along with that of Marhe et al. 2013) helps to bolster the rationale for including temptation assessments in an EMA assessment battery.

Race

Data were broken down by race to determine if White and Black cigarette smokers exhibited differences in attentional bias. The current study found no significant differences in attentional bias as a function of race on either the self-report attentional bias measure or the smoking Stroop task. Another study comparing Whites to Blacks found between-race differences on a self-report measure, but not the Smoking Stroop task (Robinson et al., 2015). Robinson et al. (2015) found Blacks reported higher attentional bias on the Subjective Attentional Bias Questionnaire (SABQ). They theorized that environmental differences between where Blacks and Whites lived may have accounted for the difference on the SABQ due to Blacks living in environments containing more smoking-related cues (Robinson et al., 2015). When the assessment involved the same number of smoking cues, as occurs during the smoking Stroop task, there is no difference in attentional bias between Whites and Blacks. It is also important to point out that the

SABQ is a multi-item assessment whereas the current study only contained a single self-report item of attentional bias.

LIMITATIONS

The study has a number of limitations. First, and perhaps most important, a relatively small number of RAs occurred before and after a temptation within the time windows of interest (<2 hours and 2-4 hours). This limited power to detect differences over time. In addition, one might question whether the parameter estimates and *p* values revealed by LMMs are valid with the small sample sizes observed in the “proximal” conditions (sample sizes were much larger in the “distal” condition). Some reassurance has been provided by simulation studies that have documented the validity of parameter estimates from linear mixed models using small sample sizes under certain conditions (Maas & Hox, 2005). Maas and Hox (2005) also noted that bootstrapping approaches could be helpful when analyzing multilevel data with small samples (Yung & Chan, 1999), and this approach could be taken in future studies examining the time course of attentional bias. Of course, missing data (e.g., random assessments that are not completed) can also potentially lead to biased parameter estimates when using LMM if the data are not missing at random. On this point, the current study included all subjects regardless of level of compliance on RAs. Although one might argue that low compliant subjects may introduce bias, excluding low compliant participants may reduce generalizability of findings. Future research can examine whether compliance moderates any of the associations reported in the current dissertation.

Second, biological measures of smoke exposure were not taken daily (they were only taken at laboratory visits), so it was not possible to verify reported abstinence on

each day. Therefore, it is not known whether participants were truly abstinent on the days identified. Future research efforts could make use of mobile CO monitors to provide an biochemical assessment of smoking in the field (Kang, 2016). In addition, smartphone based breath CO monitors may be useful to researchers (Meredith et al., 2014), and Kang (2016) reported that a commercially available expired CO monitor (iCO™) is available for use with smartphones or tablets (Bedfont Scientific Ltd., UK).

Third, to reduce participant burden during EMA, when making an entry for temptations, participants were not required to indicate the “start time” and “end time” of temptations. Therefore, as noted by Lammers (2017), it is not clear when a temptation episode actually “started”, so that the start could have occurred before the subject entry, which could complicate interpretation. Moreover, the duration of the temptation episodes in the current study is not known. Most simply, self-reported attentional bias may be elevated “after” a temptation because the temptation is still “occurring”. That said, the literature suggests the average duration of temptations is brief. Shiffman et al. (1996) reported that the median temptation duration was 11 minutes, and so it is unlikely that the elevation of self-reported attentional after the temptation reflects the fact that the assessments occur “within” the temptation.

Fourth, the study focused on the association between attentional bias and temptation episodes/craving and did not examine relationships with specific lapse episodes during EMA. As described earlier, this focus was in part due to the fact that laboratory studies have mainly used craving as an outcome variable. In addition, as noted earlier, temptations are an important outcome in their own right.

Fifth, to reduce participant burden, self-reported attentional bias was assessed with a single item. As with any single-item assessments, it was not possible to compute internal reliability for self-reported attention.

Sixth, in common with all EMA studies, and as described earlier, the act of assessment may itself cause changes in processes being measured, described as “reactivity” (Shiffman et al., 2008). Reactivity could potentially complicate data interpretation. As noted earlier, studies of reactivity in cigarette smoking studies have produced mixed results (Shiffman et al., 2002; Stone et al., 2003), and it not clear how the associations revealed in the current study could be influence by this effect. Reactivity could also influence performance on the smoking Stroop test as participants become increasingly familiar with the word sets used during the study. However, a previous study reported that associations between Stroop effects and outcomes were not moderated by time in study, suggesting that repeated exposure to the task did not influence relationships (Waters & Li, 2008)

Seventh, as noted earlier, comparisons between the results for the self-reported attentional bias and the smoking Stroop task are complicated by the presence of method differences between these two measure types. These differences mean that a direct comparison between the results for the two measures is not straightforward. Although the two measures yielded different results, it could be that these differences are, in part, an artifact of the aforementioned method differences.

Last, and as described in detail earlier, it is difficult to validate reports of self-initiated temptation assessments. This is a common challenge in EMA studies when event-based sampling involves measuring internal psychological experiences (i.e.

craving, urge, mood etc.). It is not known how many times the participants felt tempted but did not enter a TA. Therefore, it is uncertain whether the number of TAs reported during EMA reflects the “true” number of temptation episodes. As noted earlier, 21.9% of the 105 participants did not enter any TAs. It is not known whether this is because they did not experience any temptation episodes during the study period or whether those participants experience TAs but did not to enter any TAs. In any case, the sample that provide the TAs may be biased in some way potentially limiting the generality of the findings. As noted earlier, it also is unclear whether the TAs entered in the field are representative of tempted moments.

STRENGTHS

The study also has strengths. First, the study examined precipitants of temptation episodes during a highly vulnerable period within smoking cessation using EMA. Second, together with data from Lammers (2017), the study can help to provide a detailed timeline of antecedents and postcedents of temptation episodes. Last, this study provided a complimentary approach to the lab studies reviewed earlier by investigating the relationship between attentional bias and temptations episodes in the participant’s natural environment.

Public Health Impact of Findings

As noted in the introduction, tobacco use is a significant problem that may contribute to an estimated 1 billion deaths in the 21st century (World Health Organization, 2008). Great strides have been made in reducing smoking rates in the United States, but the decline in smoking rates have leveled-off (Xu et al., 2015). The number of smokers worldwide is continuing to increase as the total population increases (Ng et al., 2014).

The high number of smokers and high rate of mortality and cost of healthcare associated with cigarette smoking indicate that improving cessation rates should be an ongoing priority in public health policy both in the US and worldwide.

As described earlier, a better understanding of the psychological processes underlying relapse may lead to better interventions for smoking cessation. Cognitive biases, such as attentional bias, may promote smoking and relapse to smoking and may be a target for intervention. The public health implication of this research are as follows.

First, by tracking craving/temptations and attentional bias during quit attempts, it may ultimately be possible to identify which individuals are at risk of relapse, and when they are at risk of relapse. This idea is elaborated in the next section.

Second, if future research reveals a robust causal relationship between attentional bias and relapse, attentional bias modification may be useful and would afford clinicians with another treatment option in addition to current psychotherapy and medication interventions already available. This may be especially relevant in the US as the levelling-off of smoking rates may indicate that current treatments have reached their maximum effectiveness. An attentional bias modification treatment may align better with a patient's values and support the principles of evidence-based medicine. While some individuals respond well to medication or cessation-focused psychotherapy, low abstinence rates following treatment indicate that these treatments are not effective for everyone. Cognitive variables such as attentional bias represents another treatment target that current treatments do not address. Attention bias modification may be an effective adjunctive treatment to established cessation interventions. Incorporating attentional bias modification into an individualized cessation treatment plan may result in improved

effectiveness of cessation interventions. Utilizing multiple treatments may also have synergistic, rather than simply additive, effects resulting in improved cessation outcomes.

Third, attentional bias tracking and attentional bias modification are relatively cheap and may prove to be more easily implemented and adhered to than contemporary treatments. Some individuals are adverse to medication and low adherence to medication is a major problem in the United States (Hufford, 2007). While psychotherapy can be an effective smoking cessation treatment, there is a lingering stigma surrounding mental health care and access to care can be an issue in rural and poor regions. Also, traveling to and attending psychotherapy sessions can be a logistical and practical concern for individual who work non-standard hours or have poor access to transportation.

Interventions delivered by mobile devices such as smartphones are practical because the majority of adults already have access to a smartphone and utilize their smartphone frequently throughout the day (Insel, 2017). Smartphone applications could be constructed so direct feedback is provided on a regular basis with patients attempting to quit smoking, as opposed to receiving feedback once a week at psychotherapy appointments or once a year while seeing one's general practitioner. A trained technician could be the point of contact for multiple individuals utilizing smart-phone based attention bias modification treatments. Physicians or psychologists could supervise multiple technicians in order to improve access to treatment and the overall number of individuals completing cessation treatments.

In sum, approximately 43 million Americans continue to smoke, and the number of smokers worldwide continues to rise. There is a need for new interventions, particularly those that can be disseminated to large numbers of individuals. Although the

research described in this dissertation is in its infancy, research on cognitive processes associated with craving and relapse on mobile may ultimately help to develop new treatments for smoking cessation that could benefit public health.

FUTURE RESEARCH DIRECTIONS

One methodological question for future research is whether researchers should continue to collect data from temptation episodes (rather than simply relying on “continuous” craving data from random assessments). Although temptation episodes have been widely used in EMA research in addiction (Shiffman, 2009), there are limitations. First, and most simply, as noted earlier it is difficult to verify reports of temptations. Second, asking participants to make temptation entries (as well as lapse episodes) increases participant burden. Third, one could argue that because TAs are self-initiated and RAs are “device-initiated”, assessment type is confounded with mode of data entry. (One way around this issue would be to have participants make self-initiated assessments when not tempted to smoke). Fourth, as noted earlier, there is no way to assess whether recorded temptations are representative of the population of temptations, potentially undermining comparisons with random assessments (for which there are also missing data and questions regarding representativeness).

On the other hand, the following data support the use of temptation episodes. First, participants do appear willing to make temptation entries (and many of them). Second, if temptations were not assessed presumably investigators would miss many episodes of high craving. Third, attentional bias at TAs (rather than RAs) seems more strongly associated with relapse, at least with the drug Stroop task. Large scale investigations comparing the predictive validity of studies with and without temptation

episodes are required to determine the relative merit of the two approaches. For example, if studies using temptation episodes were better able to predict the occurrence and timing of relapse, this would bolster the case for retaining them.

If retained, future studies can continue to investigate how changes in attentional bias and other psychological variables during a cessation attempt predict subsequent temptations. In particular, additional variables such as stress and negative affect should be added to determine if one can build a multivariable model of temptation occurrence that uses all the data available in the EMA protocol. For example, as noted earlier, stress/negative affect is elevated prior to a temptation (Lammers, 2017). It may be useful to build multivariable models that examine prediction of temptations (and craving) from both attentional bias and stress/negative affect.

In the current study, the author elected to subset to days where there was no smoking and only conduct analysis using temptations. In future research with larger sample sizes, it may be useful to utilize lapses since this is the occurrence of most importance in cessation studies. Ultimately, further research can help researchers develop a predictive algorithm capable of identifying periods of heightened relapse risk. This algorithm could be applied to real life situations to identify when individuals are at risk of relapse, potentially allowing for ecological momentary interventions to be delivered in real time, when participants are most in need of the intervention.

Moreover, developments in computational algorithms and machine learning allows for new methods to predict outcomes during EMA. For example, researchers have tested three types of machine learning algorithms (Bayes, discriminant analysis and decision tree learning methods) to determine which, if any, were capable of predicting

smoking urges during a cessation attempt (Dumortier, Beckjord, Shiffman, & Sejdic, 2016). Similar to the previous EMA studies of smoking and smoking cessation, this dataset contained information on a number of smoking-related variables, including urge, smoking behaviors, and mood. The researchers found that all three machine learning approaches were able to correctly classify smoking urges with reasonable sensitivity and specificity. Based on these findings, the authors predict that algorithms developed from machine learn principles could be ultimately programmed into smartphones to predict when an individual would experience periods of vulnerability (high smoking urges) during cessation attempts (Dumortier et al., 2016).

Perhaps even more important, future studies might benefit from using a new approach, termed “digital phenotyping”, to assess behavior, mood, and cognition using mobile devices that does not require participants to report directly on these variables. With the proliferation of smartphone ownership, researchers are studying how information gathered from smartphone sensors, keyboard interaction, and voice and speech can “unobtrusively” assess mood and cognition (Insel, 2017; Jain, Powers, Hawkins, & Brownstein, 2015). Researchers are hopeful that this data may allow for better diagnosis of and assessment for psychiatric conditions because information is gathered both continuously and passively using a device that nearly 200 million adults in the United States already own (Insel, 2017).

Currently, the extent to which “digital phenotyping” may change how psychiatric conditions are measured and diagnosed is unknown. However, the results of early proof of concept studies have shown that information derived from smartphone use may be useful in treating insomnia, bipolar disorder, and depression (Jain et al., 2015). The

information provided by digital phenotyping may either complement, or replace, data gained using EMA methods. It seems the former is more likely as it is not clear how craving and attention to smoking cues could be derived from “routine” interactions with a smartphone (although information may be present in verbal data). The expectation is that this methodology (digital phenotyping allied with machine learning approaches) would be useful to apply to smoking cessation by helping to identify individuals who are at risk of relapse, and when they are at risk of relapse.

Table 1: Types of Study Examining Association between Attentional Bias and Craving

Study Design	Relationship	Lab	Field
Correlational	AB ↔ Craving	1	2
Experimental	AB → Craving	3	4
	Craving → AB	5	6

Note: Types of study that have examined the relationship between attentional bias (AB) and craving. Some studies have used a correlational design in which attentional bias is correlated with craving, either at the same time-point, or at some other point. Other studies have used an experimental approach. In some studies, AB has been manipulated as an independent variable (using attentional bias modification) and examined the effect on craving (the dependent variable). In other studies, craving has been manipulated as an independent variable (using, for example, a deprivation manipulation), and examined the effect on attentional bias (the dependent variable). Some studies have occurred in the lab, and some in the field. Numbers refer to study types that are referenced in the text.

Table 2: Lab studies Examining the Association between Attentional Bias and Craving

Author/Year	IV→ DV	Participants	IV	DV	Results	Notes
Mogg and Bradley 2002	Attentional Bias → Craving	Smokers: 13 male 14 female	2 levels: 12-hour deprivation vs. smoking ad lib 2 levels: neutral vs. smoking-related stimuli Smoking Stroop, Visual probe	Craving	Participants experienced significant attentional bias on both tasks (not increased by deprivation). Correlation between attentional bias and craving, $r=.35$	Stroop and VP performance not related, may tap different cognitive areas. Urge/wanting more closely associated with attentional bias than deprivation.
Mogg et al 2005	Attentional Bias → Craving	Smokers: 20 male 21 female	Eye tracking measures of attentional bias	Craving	Longer gaze times at smoking pictures were associated with higher levels of craving, $r=.3$	Study shows correlation between eye movement measures of attentional bias and self-reported craving
Waters et al 2003	Attentional Bias → Craving	Smokers undergoing cessation attempt: 158 (35 mg nicotine patch vs. placebo patch)	Smoking Stroop task	Craving	No significant correlation between attentional bias and craving, $r=.16$	Individual differences in smoking Stroop performance predicted lapses to smoking.

Note: Selected studies that have examined the correlation between attentional bias and craving in the laboratory (Box 1 in Table 1). All studies were reviewed in the meta-analysis of Field et al. (2009).

Table 3: Lab studies Examining Effect of ABM on Craving

Author/Year	IV→ DV	Participants	IV	DV	Results	Notes
Attwood et al 2008	ABM→ Craving	Non-treatment seeking smokers: 31 male 34 female	Visual probe task group assignment, 2-levels: “Attend” group & “Avoid” group	Attentional bias, STAI, QSU, VAS of mood items	ABM increased bias in attend group and decreased bias in avoid group. Greater increase in craving post-exposure in “attend” group (males only)	First study to report an effect of ABM on craving
Begh et al 2015	ABM → Craving	Non-treatment seeking smokers trying to quit: 49 male 69 female	Visual probe group assignment: retraining & placebo conditions	Attentional bias, craving	At 4-weeks post-quit, bias slightly lower in retraining group (but non-significant). No effect of ABM on craving.	This study used more sessions, but fewer trials per session on VP task. No attentional bias at baseline.
Field et al 2009	ABM → Craving	Non-treatment seeking smokers: 39 male 33 female	Visual probe group assignment: “Attend”, “Avoid”, & “Control”	Attentional bias, craving, smoking behaviors	ABM resulted in significant changes in attentional bias. No effect on craving and smoking.	Changes in bias occurred as expected, but changes did not persist when reassessed the next day.
Lopes et al 2014	ABM → Craving	Smokers trying to quit: 35 male 54 female	Visual probe group assignment: “Avoid 3”, “Avoid 1”, and “Avoid 0”	Attentional bias, craving (QSU)	Smokers in Avoid 1 and Avoid 3 had reduced bias after training. Avoidance was stronger as SOA increased. No effect on craving	First study to demonstrate long-term utility of ABM tasks. Number of ABM sessions influenced magnitude of bias change.
McHugh et al 2010	ABM → Craving	Non-treatment seeking smokers: 40 male 24 female	Visual probe group assignment: active vs. control training	Attentional bias, craving (QSU)	Attentional bias did not change after 1 session of retraining. No effect of craving	Slight (non-significant) reduction in bias in active group. However, neither group demonstrated baseline bias towards cigarette cues.

Note: Selected studies that have examined the effect of Attentional Bias Modification (ABM) on attentional bias and craving in the laboratory in smokers (Box 3 in Table 1). QSU = Questionnaire for Smoking Urges (a craving assessment)

Table 4: Descriptive Statistics for Abstinent Days Comparing TAs and RAs

<i>Assessment Type→</i>	RA	RA	RA	TA	RA	RA	RA		All RAs
<i>Time→</i>	Before	Before	Before		After	After	After		
<i>Hours→</i>	4+	2-4	0-2		0-2	2-4	4+		
Self-reported bias (1-7)	$n_I=1090$	$n_I=31$	$n_I=41$	$n_I=221$	$n_I=37$	$n_I=47$	$n_I=1078$		$n_I=1162$
	2.72	3.35	3.24	3.39	3.19	3.55	2.70		2.75
	(1.73)	(1.94)	(2.06)	(2.05)	(2.01)	(2.06)	(1.72)		(1.75)
Stroop effect (ms)	$n_I=427$	$n_I=13$	$n_I=13$	$n_I=81$	$n_I=13$	$n_I=18$	$n_I=422$		$n_I=453$
(uninterrupted assessments)	13.32	14.58	-33.73	-17.65	-11.42	-31.61	14.59		12.00
	(100.69)	(35.28)	(146.05)	(110.42)	(70.82)	(97.78)	(101.66)		(101.08)
Stroop effect (ms)	$n_I=629$	$n_I=22$	$n_I=20$	$n_I=125$	$n_I=18$	$n_I=27$	$n_I=626$		$n_I=671$
(all assessments)	16.76	-24.80	0.75	-2.40	-9.39	-21.33	17.19		14.92
	(112.44)	(137.99)	150.15	(109.13)	(74.30)	(123.46)	(115.27)		(114.66)

Note: Data are Mean (SD) aggregated over all assessments. Data are from abstinent days. Data from all subjects are included. Uninterrupted assessments are those in which the participant reported no interruptions when completing the smoking Stroop task (see text for details). n_I = number of level 1 observations (assessments). RA = Random Assessment, TA = Temptation Assessment

Table 5: Descriptive Statistics for Abstinent Days Comparing Maximum Craving Assessments with Other Assessments

<i>Craving Level</i> →	≤6	≤6	≤6	7	≤6	≤6	≤6	All ≤6
<i>Time</i> →	Before	Before	Before		After	After	After	
<i>Hours</i> →	4+	2-4	0-2		0-2	2-4	4+	
Self-reported bias (1-7)	$n_I=1290$	$n_I=19$	$n_I=14$	$n_I=130$	$n_I=11$	$n_I=18$	$n_I=1294$	$n_I=1323$
	2.65	4.42	3.86	5.07	3.55	4.72	2.66	2.69
	(1.66)	(1.71)	(2.07)	(1.91)	(1.92)	(1.60)	(1.66)	(1.68)
Stroop effect (ms)	$n_I=532$	$n_I=7$	$n_I=7$	$n_I=50$	$n_I=3$	$n_I=8$	$n_I=535$	$n_I=546$
(uninterrupted assessments)	10.58	54.00	31.14	25.31	-13.33	7.38	11.60	11.40
	(101.65)	(79.85)	(65.15)	(117.44)	(30.99)	(135.74)	(100.87)	(101.06)
Stroop effect (ms)	$n_I=780$	$n_I=9$	$n_I=10$	$n_I=72$	$n_I=6$	$n_I=13$	$n_I=780$	$n_I=799$
(all assessments)	14.19	1.44	48.10	19.34	3.42	-3.27	14.85	14.46
	(112.11)	(136.78)	(102.47)	(123.66)	(113.43)	(120.89)	(112.18)	112.21

Note: Data are Mean (SD) aggregated over all assessments. Data are from abstinent days. Data from all subjects are included. Uninterrupted assessments are those in which the participant reported no interruptions when completing the smoking Stroop task (see text for details). n_I = number of level 1 observations (assessments). Maximum craving = 7 (1-7 scale), Non-Maximal craving = 1-6 (1-7 scale).

Table 6: Descriptive Statistics for Abstinent Days Comparing “High” craving assessments with “Low” craving assessments

<i>Craving Level</i> →	≤4	≤4	≤4	5-7	≤4	≤4	≤4		All ≤4
<i>Time</i> →	Before	Before	Before		After	After	After		
<i>Hours</i> →	4+	2-4	0-2		0-2	2-4	4+		
Self-reported bias (1-7)	$n_I=906$	$n_I=42$	$n_I=19$	$n_I=486$	$n_I=21$	$n_I=33$	$n_I=913$		$n_I=967$
	2.09	3.55	3.47	4.34	3.19	3.15	2.12		2.18
	(1.32)	(1.64)	(1.93)	(1.75)	(1.69)	(1.33)	(1.37)		(1.40)
Stroop effect (ms)	$n_I=357$	$n_I=19$	$n_I=6$	$n_I=214$	$n_I=4$	$n_I=15$	$n_I=363$		$n_I=382$
(uninterrupted assessments)	4.75	45.89	21.58	22.39	27.63	5.77	6.89		7.06
	(100.54)	(75.74)	(72.13)	(107.45)	(42.30)	(86.87)	(100.37)		(99.34)
Stroop effect (ms)	$n_I=522$	$n_I=28$	$n_I=13$	$n_I=308$	$n_I=10$	$n_I=21$	$n_I=532$		$n_I=563$
(all assessments)	13.21	43.23	35.73	14.23	74.35	55.10	12.53		15.22
	(112.07)	(81.95)	(135.15)	(116.43)	(128.93)	(152.38)	(108.81)		(111.39)

Note: Data are Mean (SD) aggregated over all assessments. Data are from abstinent days. Data from all subjects are included. Uninterrupted assessments are those in which the participant reported no interruptions when completing the smoking Stroop task (see text for details). n_I = number of level 1 observations (assessments). “High” craving = 5-7 (1-7 scale), “Low” craving = 1-4 (1-7 scale).

Table 7. Results of Linear Mixed Models for Specific Aims 1, 2, and 3 Comparing TAs with RAs

Aim	DV →	H	Self-Reported Attentional Bias						Stroop				
	IV ↓		<i>df</i>	<i>PE</i>	<i>SE</i>	<i>F</i>	<i>p</i>		<i>df</i>	<i>PE</i>	<i>SE</i>	<i>F</i>	<i>p</i>
1	TA vs. RA	1	1, 59.02	0.74	0.16	21.11	.001		1, 575.10	-6.75	11.48	0.34	.203
2	T1 vs. Control	2	1, 363.76	0.15	.21	0.53	.468		1, 183.75	-25.22	31.75	0.63	.428
	T2 vs. Control	2	1, 371.43	0.28	.25	1.25	.264		1, 173.75	18.99	29.50	0.41	.521
	(T1 & T2) vs. Control	2	1, 948.60	0.27	.15	3.18	.075		1, 449.33	-21.75	21.49	1.02	.312
3	T1 vs. Control	3	1, 487.82	0.33	.20	2.62	.106		1, 220.56	-31.37	32.33	0.94	.333
	T2 vs. Control	3	1, 507.18	0.54	.19	8.22	.004		1, 223.04	-51.78	28.29	3.35	.069
	(T1 & T2) vs. Control	3	1, 934.21	0.48	.14	11.58	.001		1, 462.45	-40.50	20.50	3.91	.049

Note: Data are results of linear mixed models. H = Hypothesis; *PE* = parameter estimate; *SE* = standard error; *F* = F value from LMM; T1 reflects RAs occurring within 2 hours of a TA (before or after); T2 reflects RAs occurring between 2-4 hours of a TA (before or after); Control reflects RAs occurring more than 4 hours from a TA. Number of assessments range from 471 to 1383 for Self-Reported Attentional Bias, and from 193 to 534 for the Smoking Stroop effect. Data from smoking Stroop effect reflect uninterrupted assessments. Parameter estimates reflect within-subject effects (between-subject effects not shown). T1 vs Control compares RAs within 2 hours of a TA (before or after) with Control RAs. T2 vs Control compares RAs occurring between 2-4 hours of a TA (before or after) with Control RAs. (T1 & T2) vs. Control compares RAs within 4 hours of a TA (before or after) with Control RAs.

Table 8. Results of Linear Mixed Models for Exploratory Analysis of “Maximal” Craving

	DV →			Self-Reported Attentional Bias						Stroop				
Aim	IV ↓	H		<i>df</i>	<i>PE</i>	<i>SE</i>	<i>F</i>	<i>P</i>		<i>df</i>	<i>PE</i>	<i>SE</i>	<i>F</i>	<i>p</i>
1	CR7 vs. CR1-6	1		1, 36.80	1.07	0.26	16.70	.001		1, 567.75	4.15	18.42	0.05	.822
2	T1 vs. Control	2		1, 169.01	-0.14	0.40	0.12	.729		1, 81.33	17.64	40.04	0.19	.661
	T2 vs. Control	2		1, 176.61	0.47	0.36	1.73	.191		1, 73.20	6.57	37.77	0.030	.862
	(T1 & T2) vs. Control	2		1, 1212.21	0.24	0.22	1.22	.269		1, 528.71	23.18	27.32	0.72	.397
3	T1 vs. Control	3		1, 294.78	-0.39	0.44	0.76	.384		1, 137.44	-34.65	55.31	0.39	.532
	T2 vs. Control	3		1, 309.63	0.45	0.34	1.77	.185		1, 138.28	6.39	37.08	0.03	.863
	(T1 & T2) vs. Control	3		1, 1161.84	0.55	0.22	5.93	.015		1, 503.32	-4.12	32.00	0.02	.898

Note: Data are results of linear mixed models. H = Hypothesis; *PE* = parameter estimate; *SE* = standard error; *F* = F value from LMM; T1 reflects RAs occurring within 2 hours of an assessment with maximal craving (before or after); T2 reflects RAs occurring between 2-4 hours of an assessment with maximal craving (before or after). Control reflects non-maximal craving assessments (craving 1-6) occurring more than 4 hours from an assessment with maximal craving (craving = 7). Number of assessments range from 222 to 1453 for Self-Reported Attentional Bias, and from 107 to 596 for the Smoking Stroop effect. Data from smoking Stroop effect reflect uninterrupted assessments. T1 vs Control compares non-maximal craving assessments within 2 hours of a maximal craving assessment (before or after) with Control assessments. T2 vs Control compares non-maximal craving assessments occurring between 2-4 hours of a maximal craving assessments (before or after) with Control assessments. (T1 & T2) vs. Control compares non-maximal craving assessments within 4 hours of a maximal craving assessment (before or after) with Control assessments.

Table 9. Results of Linear Mixed Models for Exploratory Analysis of “High” Craving

	DV →			Self-Reported Attentional Bias						Stroop				
Aim	IV ↓	H		<i>df</i>	<i>PE</i>	<i>SE</i>	<i>F</i>	<i>P</i>		<i>df</i>	<i>PE</i>	<i>SE</i>	<i>F</i>	<i>p</i>
1	CR5-7 vs. CR1-4	1		1, 73.40	0.82	0.15	31.99	.001		1, 570.82	-.372	12.23	0.00	.976
2	T1 vs. Control	2		1, 275.93	0.48	0.28	2.96	.087		1, 102.23	26.16	35.89	0.53	.468
	T2 vs. Control	2		1, 279.13	0.53	0.21	6.76	.010		1, 137.33	44.02	23.19	3.60	.060
	(T1 & T2) vs. Control	2		1, 857.06	0.48	0.15	9.80	.002		1, 361.34	40.19	21.02	3.65	.057
3	T1 vs. Control	3		1, 428.62	0.12	0.27	0.19	.661		1, 167.14	27.52	46.68	0.35	.556
	T2 vs. Control	3		1, 417.32	0.49	0.22	4.97	.026		1, 179.76	4.87	27.83	0.03	.861
	(T1 & T2) vs. Control	3		1, 849.33	0.21	0.16	1.67	.196		1, 370.49	8.16	24.66	0.11	.741

Note: Data are results of linear mixed models. H = Hypothesis; *PE* = parameter estimate; *SE* = standard error; *F* = F value from LMM; T1 reflects RAs occurring within 2 hours of an assessment with high craving (before or after); T2 reflects RAs occurring between 2-4 hours of an assessment with high craving (before or after). Control reflects “low” craving assessments (craving 1-4) occurring more than 4 hours from an assessment with “high” craving (craving 5-7). Number of assessments range from 325 to 1453 for Self-Reported Attentional Bias, and from 152 to 596 for the Smoking Stroop effect. Data from smoking Stroop effect reflect uninterrupted assessments. T1 vs Control compares “low” craving assessments within 2 hours of a “high” craving assessment (before or after) with Control assessments. T2 vs Control compares “low” craving assessments occurring between 2-4 hours of a “high” craving assessments (before or after) with Control assessments. (T1 & T2) vs. Control compares “low” craving assessments within 4 hours of a “high” craving assessment (before or after) with Control assessments.

Table 10. Results of Lagged Analyses For the Association between Attentional Bias and Assessment Type

	DV →			Assessment Type (time t_{+1})						Attentional Bias (time t_{+1})				
Analysis	IV ↓	DV		df	PE	SE	F	p		df	PE	SE	F	p
1	Lagged Explicit (t)	Assessment Type (t_{+1})		1, 76.24	-0.01	0.01	0.52	.47		n/a	n/a	n/a	n/a	n/a
2	Lagged Stroop (t)	Assessment Type (t_{+1})		1, 434.7	-0.00	0.00	0.01	.92		n/a	n/a	n/a	n/a	n/a
3	Lagged Assessment Type (t)	Explicit (t_{+1})		n/a	n/a	n/a	n/a	n/a		1, 68.88	0.40	0.14	7.93	.006
4	Lagged Assessment Type (t)	Stroop (t_{+1})		n/a	n/a	n/a	n/a	n/a		1, 57.24	-27.76	16.37	2.88	.10

Note: Data are results of linear mixed models for “lagged analyses” for the association between attentional bias and assessment type (see text for details); *PE* = parameter estimate; *SE* = standard error; *F* = F value from LMM; Explicit = Self-Reported Attentional Bias. Number of assessments range from 468 to 952. Only assessments occurring on the same day as the previous assessment were included in analyses (see text for details). Explicit = Self-reported attentional bias. Assessment Type = RA (random assessment) vs. TA (temptation assessment). Stroop = Smoking Stroop effect.

Table 11. Results of Lagged Analyses For the Association between Attentional Bias and Craving

	DV →			Craving (time t_{+1})						Attentional Bias (time t_{+1})				
Analysis	IV ↓	DV		df	PE	SE	F	p		df	PE	SE	F	p
1	Lagged Explicit (t)	Craving (t_{+1})		1, 76.12	0.09	0.04	4.65	.034		n/a	n/a	n/a	n/a	n/a
2	Lagged Stroop (t)	Craving (t_{+1})		1, 433.35	0.00	0.0005	0.06	.804		n/a	n/a	n/a	n/a	n/a
3	Lagged Craving (t)	Explicit (t_{+1})		n/a	n/a	n/a	n/a	n/a		1, 76.32	0.17	0.05	13.03	.001
4	Lagged Craving (t)	Stroop (t_{+1})		n/a	n/a	n/a	n/a	n/a		1, 37.2	1.35	10.20	0.02	.902

Note: Data are results of linear mixed models for “lagged analyses” between attentional bias and craving (see text for details); *PE* = parameter estimate; *SE* = standard error; *F* = F value from LMM; Explicit = Self-Reported Attentional Bias. Number of assessments range from 529 to 952. Only assessments occurring on the same day as the previous assessment are included in analyses (see text for details). Explicit = Self-reported attentional bias. Craving = craving rating (1-7 scale). Stroop = Smoking Stroop effect.

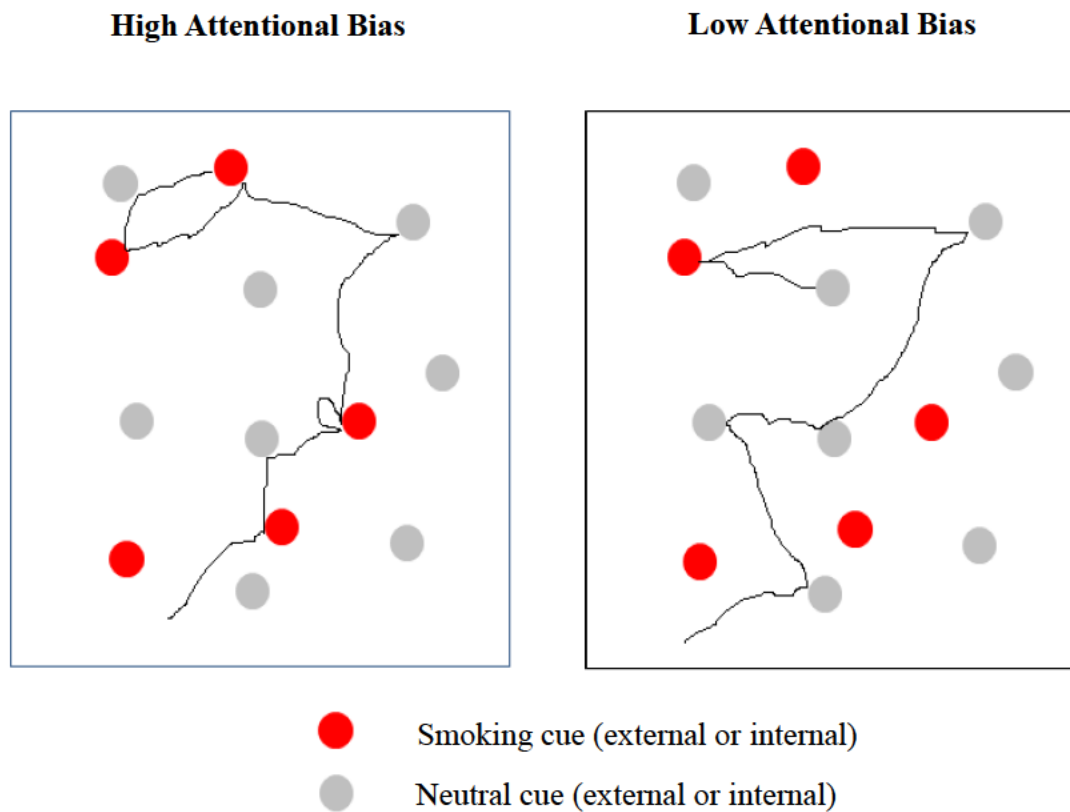


Figure 1. Illustration of eye gaze differences between smokers with High- and Low-attentional bias

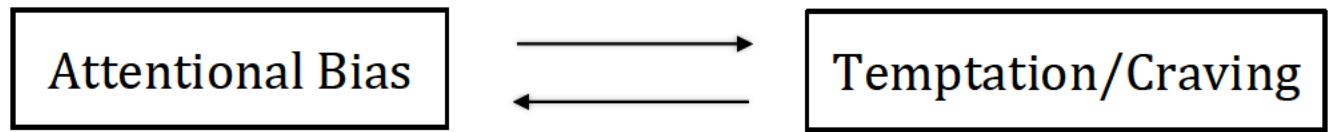


Figure 2. Conceptual model displaying theorized relationship between attentional bias and temptation.

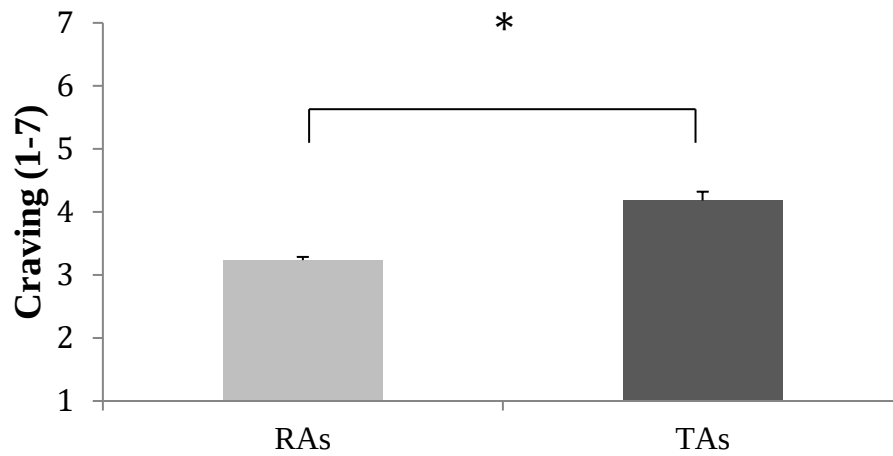


Figure 3. Effect of Assessment Type on Craving in Lammers (2017). RAs = Random Assessments; TAs = Temptation Assessments. Error bars show 1 S.E. $*p < .001$

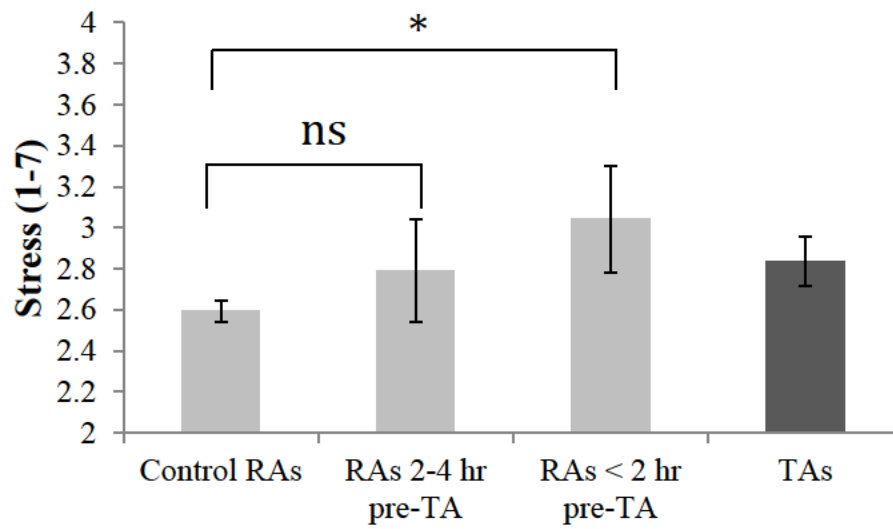


Figure 4. Stress before TAs in Lammers (2017). RAs = Random Assessments; TAs = Temptation Assessments Errors bars show 1 S.E. * $p < .05$, ns = non-significant

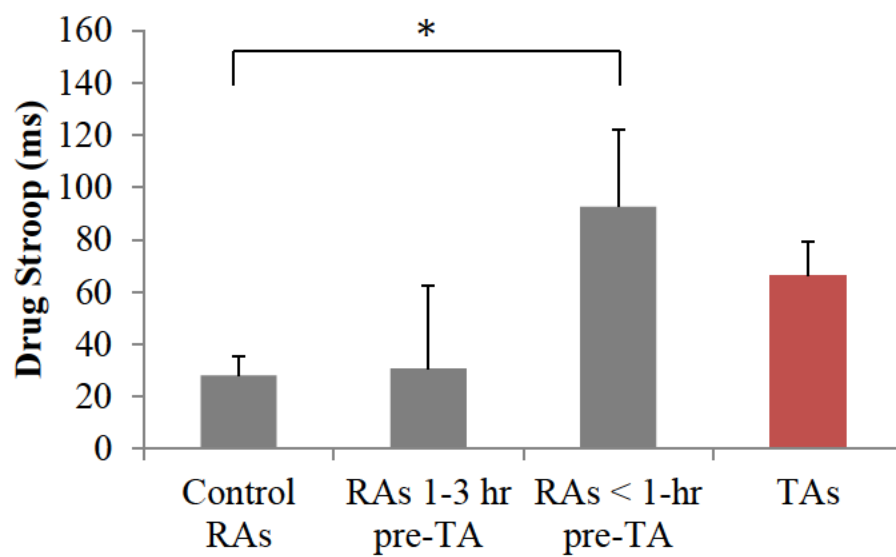


Figure 5. Attentional bias prior to TAs in Waters et al. (2012). TAs = Random Assessments; TAs = Temptation Assessments

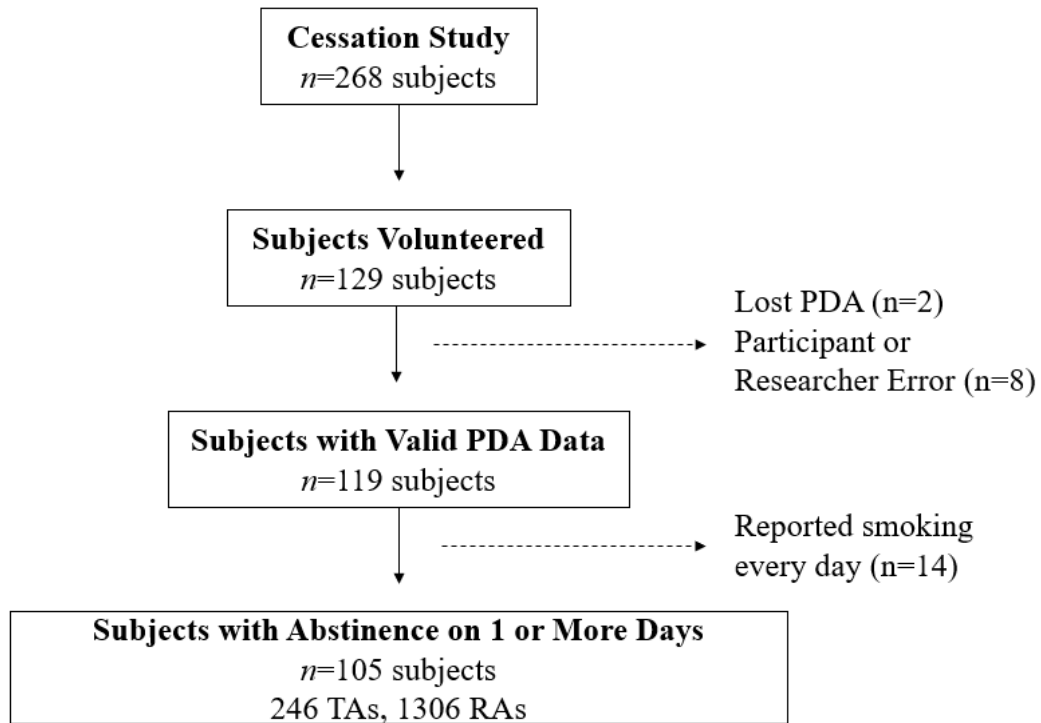


Figure 6. Consort flow chart illustrating subject numbers

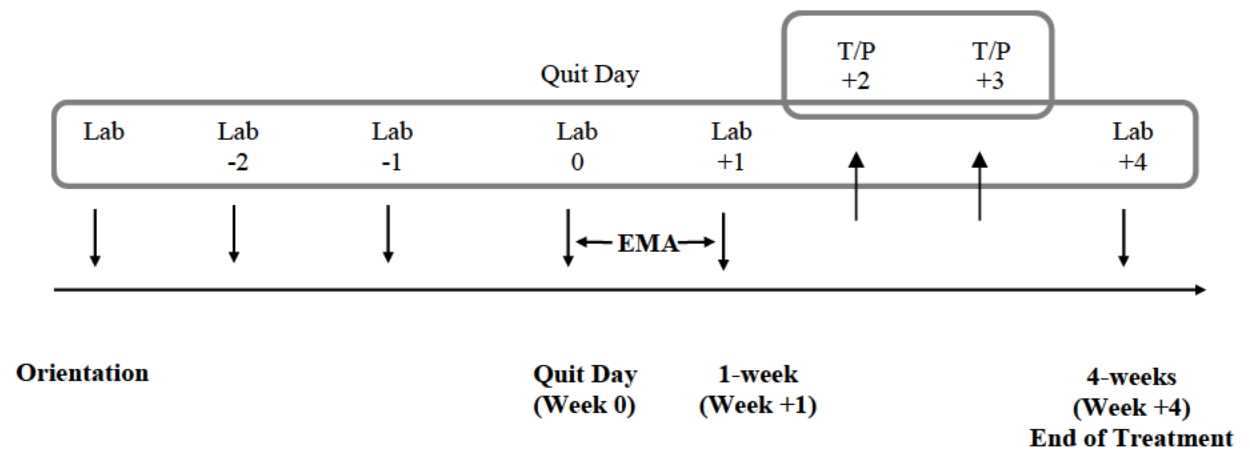


Figure 7: Overview of parent study. T/P = telephone counseling.

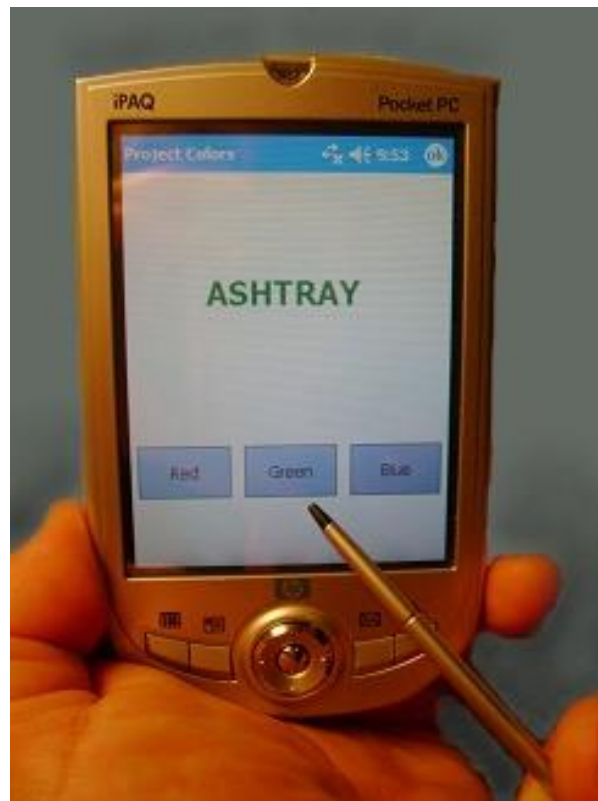


Figure 8: Screenshot of modified Stroop task presented on a PDA (Waters & Li, 2008)

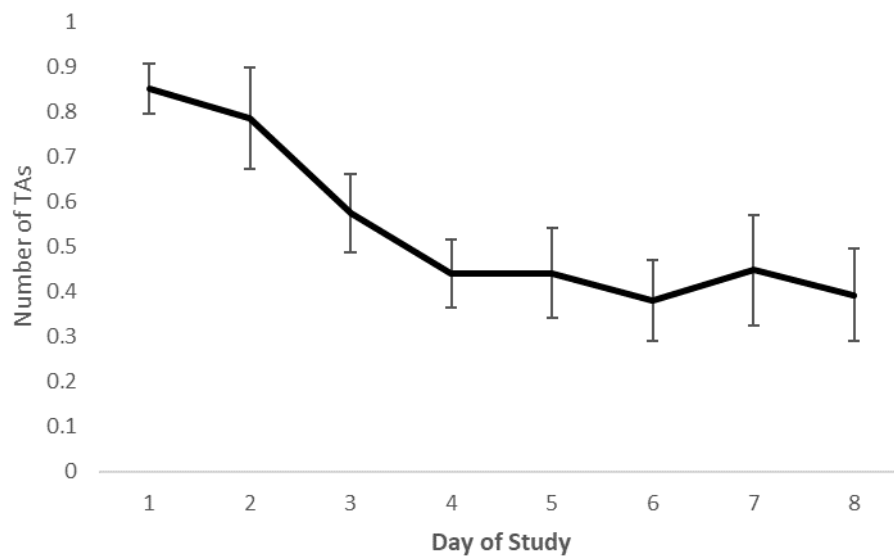


Figure 9: Graph of number of TAs over time

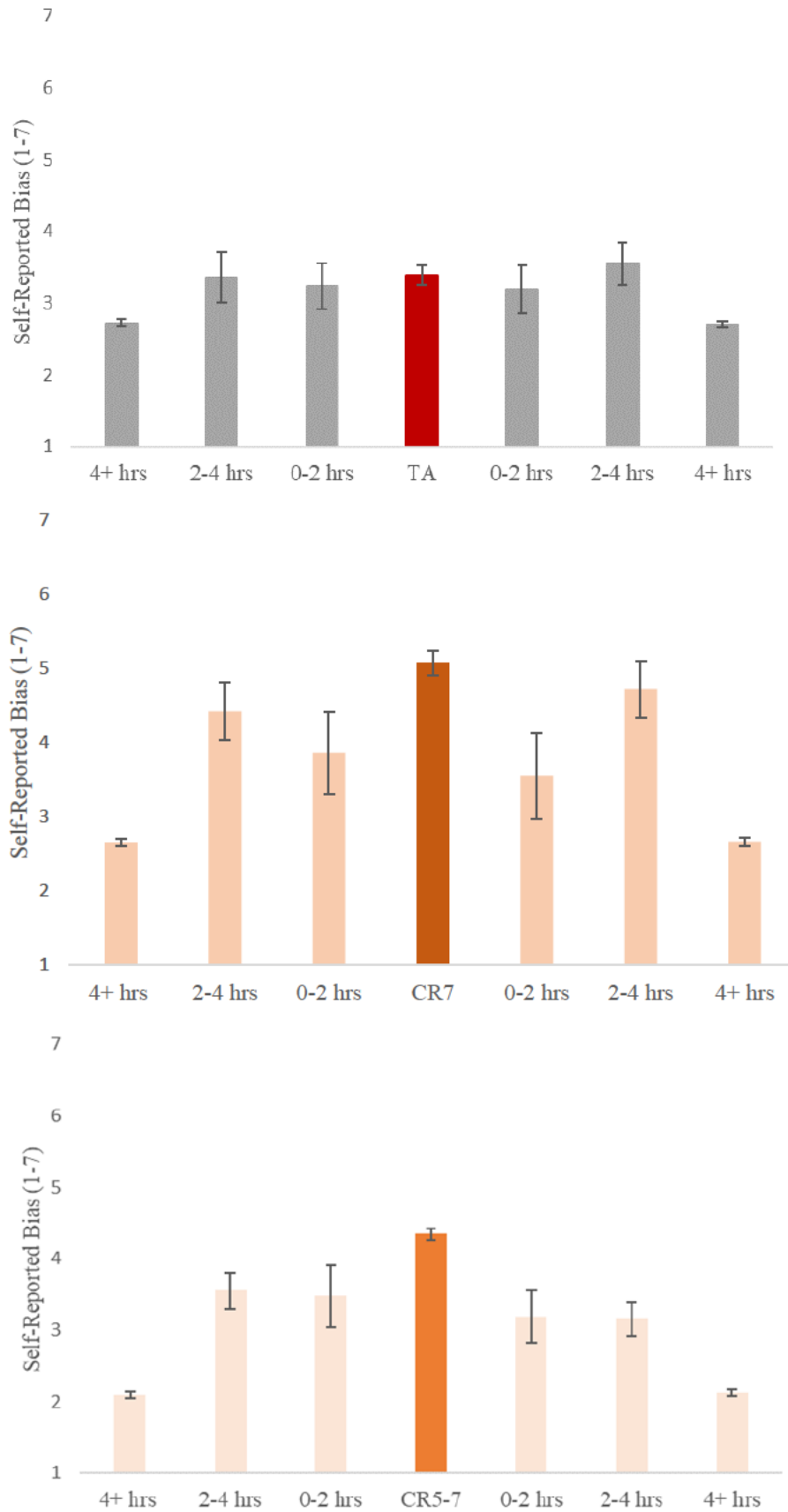


Figure 10: Timeline of self-reported attentional bias for TAs vs RAs (grey) (top), Maximal (CR7) vs Non-Maximal (CR1-6, lighter) Craving (middle), High (CR5-7) vs Low (CR1-4, lighter) Craving (bottom)

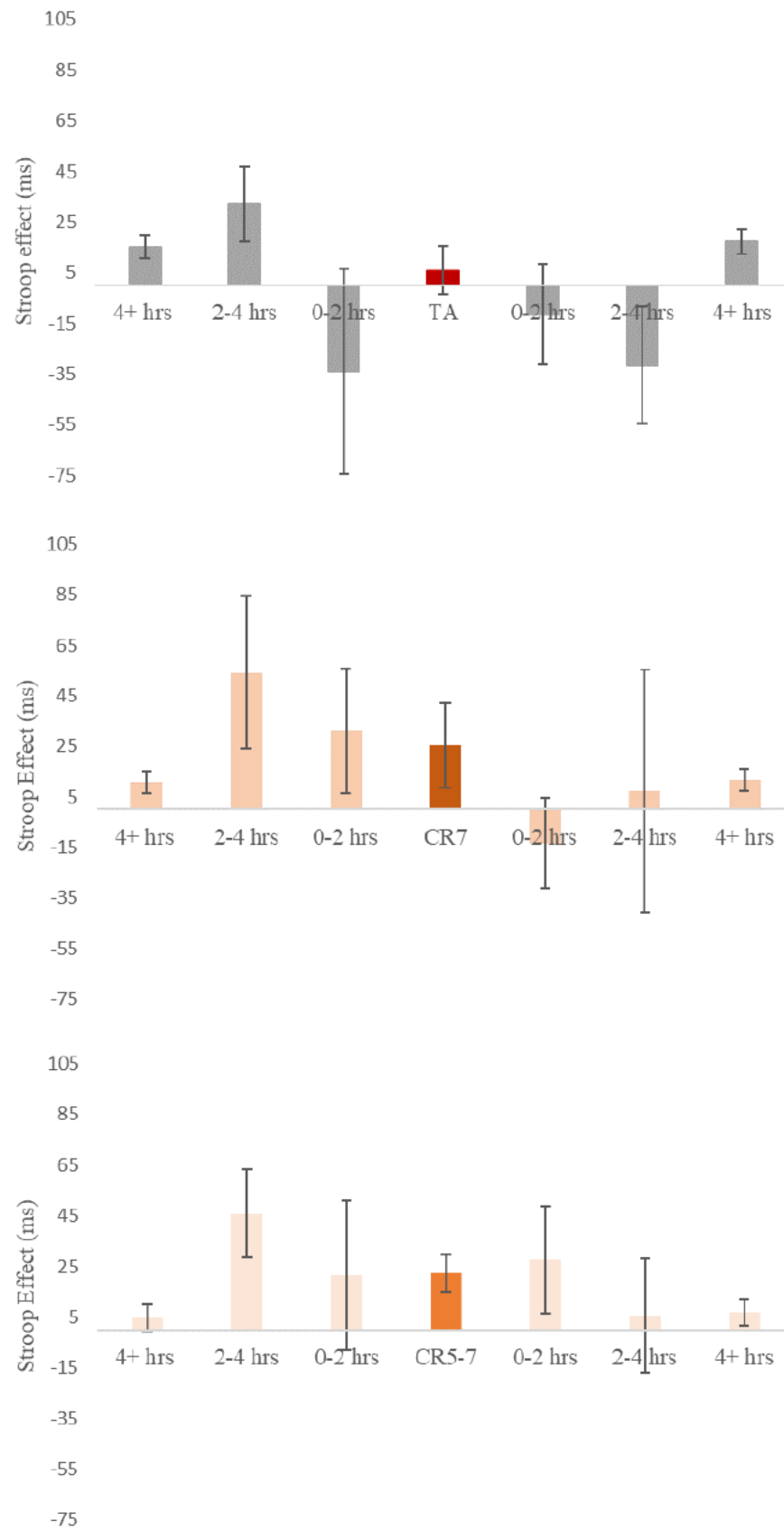


Figure 11: Timeline of smoking Stroop (uninterrupted assessments) for TAs vs RAs (top), Maximal (CR7) vs Non-Maximal (CR1-6) Craving (middle), High (CR5-7) vs Low (CR1-4) Craving (bottom)

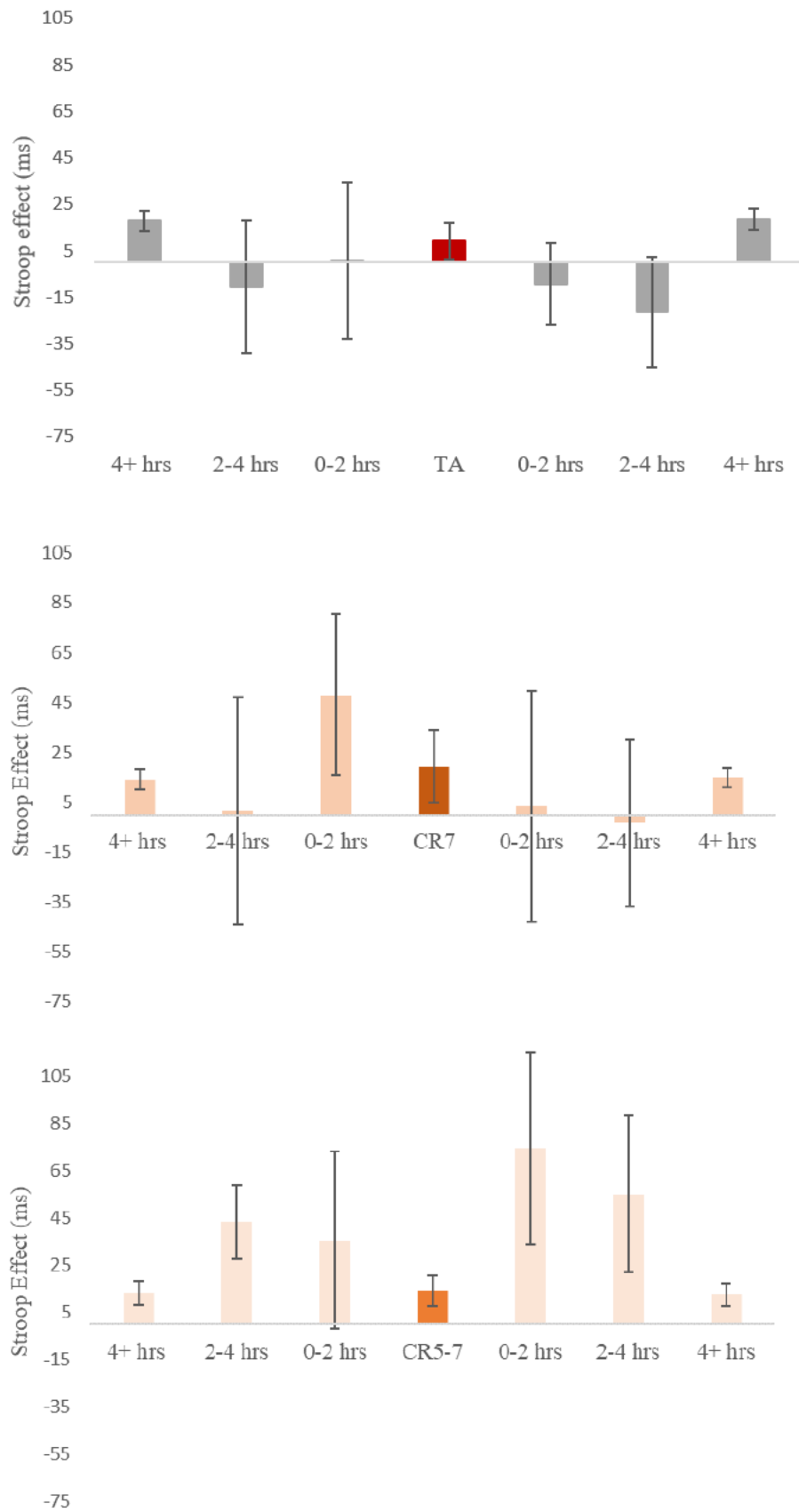


Figure 12: Timeline of smoking Stroop (all assessments) for TAs vs RAs (top), Maximal (CR7) vs Non-Maximal (CR1-6) Craving (middle), High (CR5-7) vs Low (CR1-4) Craving (bottom)

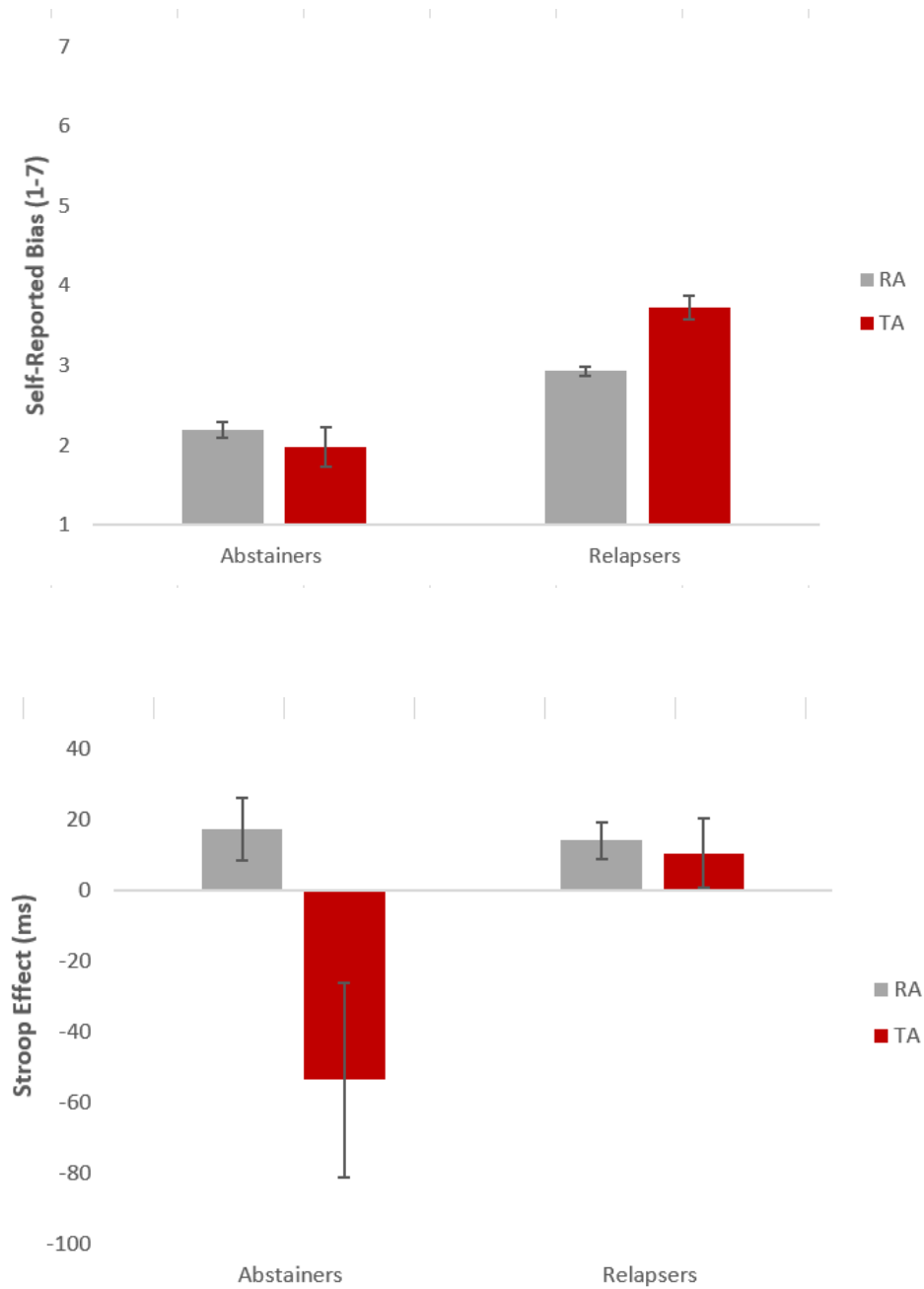


Figure 13: Self-reported Attentional Bias and smoking Stroop as function of Relapse Group at Week +4

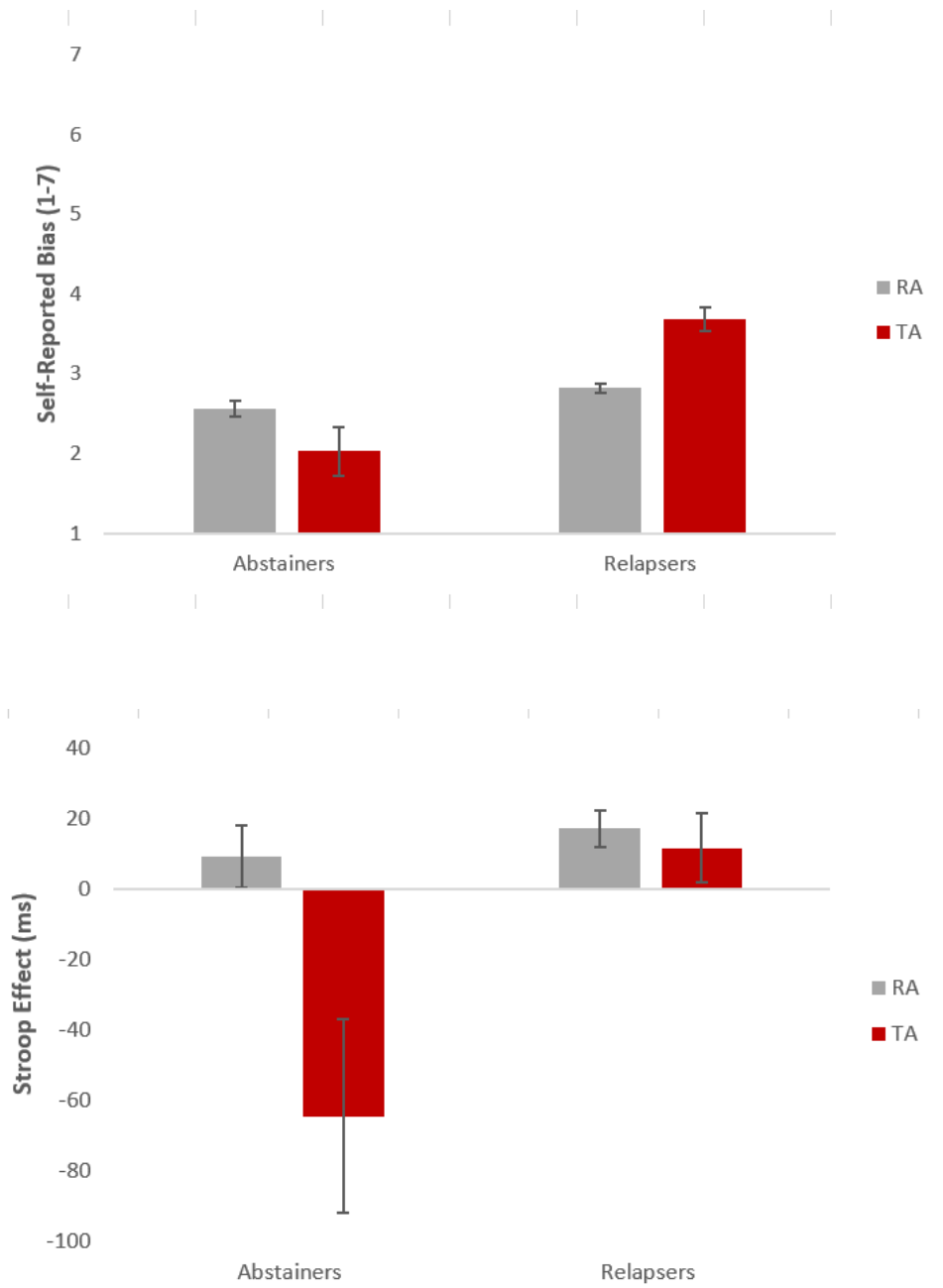


Figure 14: Self-reported Attentional Bias and smoking Stroop as function of Relapse Group at Week +1

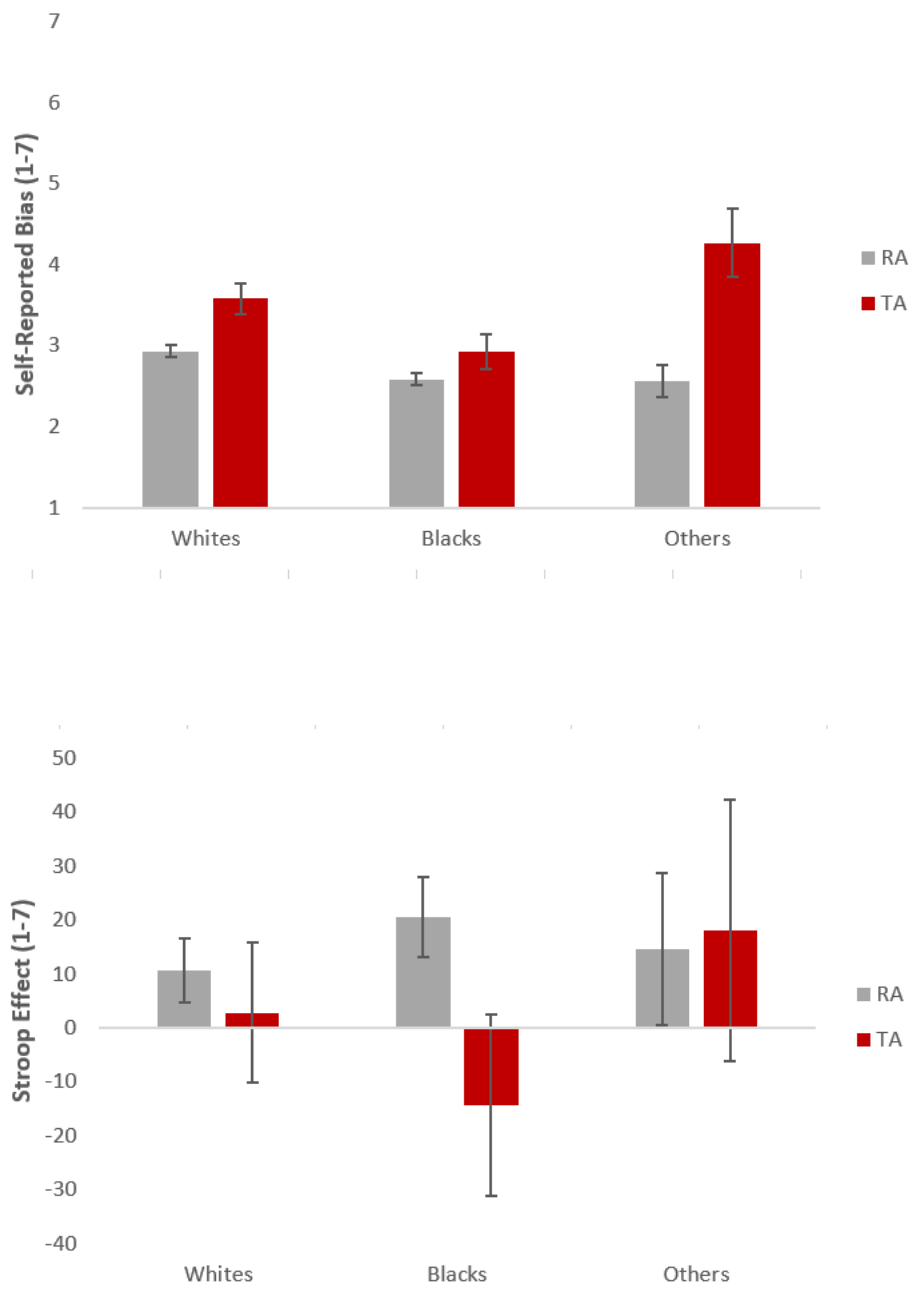


Figure 15: Self-reported Attentional Bias and smoking Stroop as function of Race



UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

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BETHESDA, MARYLAND 20814-4799
www.usuhs.mil



May 12, 2017

MEMORANDUM FOR CPT John P Lammers, P and R - Uniformed Services University of the Health Sciences (USUHS)

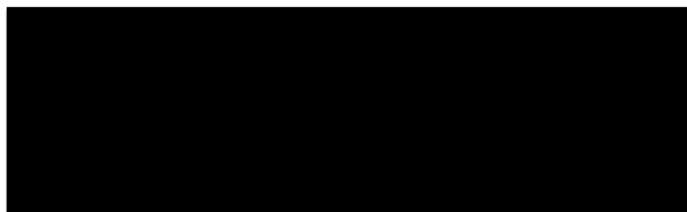
SUBJECT: USUHS IRB #1 (FWA 00001628; DoD Assurance P60001) Approval of Protocol TO-72-9031 for Human Subjects Participation

Congratulations! The Initial Review for your minimal risk human subjects research protocol TO-72-9031 entitled "*Antecedents and Possedents of Temptation During Smoking Cessation: An Ecological Momentary Assessment Study*" was reviewed and approved for execution on May 12, 2017 by Leodayan Bojanowski DNP, EDO as an EXEMPT protocol under the provision of 32 CFR 219.101(b)(4). This approval will be reported to the USUHS IRB #1 scheduled to meet on June 8, 2017.

This study is a secondary analysis of de-identified data previously collected from July 2007 to July 2011 where individuals underwent a 1-week prospective observational study of smoking cessation that used mobile devices (PDAs) to collect EMA data. This study will examine associations between attentional bias and temptation during the first week of a quit attempt. Specific aim 1 is to examine the relationship between attentional bias & assessment type (TAs vs. RAs) during attempted abstinence from smoking. Specific aim 2 is to examine whether attentional bias provokes temptations during attempted abstinence from smoking. Specific Aim 3 is to examine whether temptations provoke attentional bias during attempted abstinence from smoking.

You are required to submit amendments to this protocol, changes to the informed consent document (if applicable), adverse event reports, and other information pertinent to human research for this project. No changes to this protocol may be implemented prior to IRB approval. If you have questions regarding this IRB action or questions of a more general nature concerning human participation in research, please contact Chris Murphy at christopher.murphy.cwr@usuhs.edu or 301-319-0444.

Christopher Murphy
IRB Analyst



Appendix B: Parent Study USUHS IRB Approval



UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4790



September 8, 2009

MEMORANDUM FOR DR. ANDREW WATERS, PH.D., MEDICAL AND CLINICAL PSYCHOLOGY

SUBJECT: Uniformed Services University Institutional Review Board (FWA 00001628; DoD Assurance P60001) Approval regarding Human Subjects Research Protocol G172JY.

Congratulations! The amendment for your No More Than Minimal Risk human subjects research protocol G172JY, entitled "*Cognitive Processes in Smoking Cessation*," was reviewed and approved for execution on Tuesday, September 8, 2009 by Edmund G. Howe III, M.D., J.D., Chairperson, Uniformed Services University IRB, under the provisions of 32 CFR 219.110(b)(2). This approval will be reported to the full Uniformed Services University IRB scheduled to meet on Thursday, October 15, 2009.

The purpose of this behavioral research study is to find out which types of smokers are in need of more help with quitting smoking.

This action approves amendment #5 that: (1) adds two study personnel (CITI complete 7/18/09 and 8/13/09); (2) revises recruitment numbers up to 250 to account for participants who sign the ICD but are later deemed ineligible; (3) makes minor revisions to the ICD regarding compensation; and (4) adds venues for study advertisements (utilizing the previously approved advertisements).

Authorization to conduct protocol G172JY will automatically terminate on Tuesday, January 5, 2010. You are authorized to enroll up to 250 subjects in this study. If you plan to continue data collection or analysis beyond this date, IRB approval for continuation is required. Please submit a USU Form 3204A/B (application for continuing approval) to the IRB Office 60 days prior to the termination date. The IRB Office will attempt to assist you by sending you a reminder; however, submission of an application for continuation is your responsibility. Please note the termination date and the date for submission of your USU Form 3204A/B in your calendar!

You are required to submit amendments to this protocol, changes to the informed consent document (if applicable), adverse event reports, and other information pertinent to human research for this project to this office for review. No changes to this protocol may be implemented prior to IRB approval. If you have questions regarding this IRB action, or questions of a more general nature concerning human participation in research, please contact the undersigned at mstretch@usuhs.mil or (301) 295-0819.

[Redacted Signature]
Micah Stretch, M.A., J.D.
IRB Coordinator

cc: Chair, MPS
✓ VPROSP
File

Appendix C: MDACC Approval of Data Transfer



Office of Protocol Research

Institutional Review Board (IRB)
Unit 1437
Phone 713-792-2933
Fax 713-794-4589

To: Paul Cinciripini 03/31/2009
From: Marion B. Olson
CC: Sunetra Martinez, Victoria L. Brown, Evanna L. Thompson, Veronica Roberts
MDACC Protocol ID #: 2005-0741
Protocol Title: Cognitive Processes in Smoking Cessation
Version: 13

Subject: Administrative IRB Approval – Protocol 2005-0741

On Tuesday, 03/31/2009, the Institutional Review Board (IRB) 4 chair or designee reviewed and approved your revision dated 03/27/2009 for Protocol 2005-0741

These Pages Include:

- Protocol Body – Document header Date: 03/27/2009

Revision Included the following changes:

Clarifying that the de-identified data will be sent to Dr. Andrew Waters and his statistical team at the Uniformed Services University of the Health Sciences.

Additional Revision History:

Please note that along with this revision the M. D. Anderson IRB approves the transfer of de-identified study data for analysis to Dr. Andrew Waters, collaborator on this study, and his statistical team at the Uniformed Services University of the Health Sciences.

The revision can now be implemented. Please inform the appropriate individuals in your department or section and the collaborators of these changes.

Please inform the appropriate individuals in your department/section and your collaborators of these revisions.

Please Note: This approval does not alter or otherwise change the continuing review date of this protocol.

In the event of any questions or concerns, please contact the sender of this message at (713) 792-2933.

Marion B. Olson 03/31/2009 10:02:17 AM

This is a representation of an electronic record that was signed electronically and below is the manifestation of that electronic signature:

Marion B. Olson
03/31/2009 09:51:14 AM

IRB 4 Chair Designee
FWA #: IRB00005015

Appendix D: USUHS Informed Consent Form
This consent form is valid only if it contains the IRB stamped date

Consent for Voluntary Participation in a Non-Clinical Research Study

1. INTRODUCTION OF THE STUDY

You are being asked to be in a research study entitled, “Cognitive Processes in Smoking Cessation”, at the Uniformed Services University (USU), Bethesda, Maryland. You have been asked to take part in this study because you are a smoker, and you want to quit smoking. Your participation is voluntary. Refusal to participate will not result in any punishment or loss of benefits to which you are otherwise permitted. Please read the information below, and ask questions about anything you do not understand, before deciding whether to take part in the study.

2. PURPOSE OF THE STUDY

The purpose of this behavioral research study is to find out which type of smokers are in need of more help with quitting smoking. This study may help researchers create more effective cessation (quitting) programs. Researchers want to learn the reasons why some smokers who quit smoking choose to start up again (relapse) more quickly than other smokers. Also, researchers want to use computerized tasks to help predict who is likely to relapse.

Other studies have shown that some computerized tasks are helpful in determining which smokers are likely to relapse more quickly. We want to carry out more research using additional tests.

3. PROCEDURES TO BE FOLLOWED

If you agree to be in this study, you will be asked to attend a total of 6 sessions at USU. At the first session (orientation), you will complete a breath test that allows the investigators to know how much you smoke. You will also complete about 7 questionnaires, which will take a total of about 1 hour to complete. The questionnaires will ask about you and your health, your smoking habits, and your drinking habits. There will also be a brief reading test, which will take about 5 minutes to complete. It will check your reading ability. The orientation will help researchers learn if you are eligible to participate in this study.

If you are found to be eligible and you wish to take part in this study, you will attend 5 laboratory sessions at USU. You will attend 2 sessions before trying to quit, 1 session on your quit day, 1 session one week after your quit day, and a final session 1 month after your quit day. At each of these laboratory sessions, you will complete a series of computerized evaluations, which will take about 90 minutes to complete. These evaluations are reaction-time tests.

At the 2 pre-quit sessions, you will be asked to smoke a cigarette (after the computerized evaluation). Before one of these pre-quit sessions, which will be picked randomly, you will be asked to stop smoking for 12 hours before the session.

During each of the laboratory sessions, you will also complete about 7 questionnaires that ask about your mood, cigarette cravings, and smoking habits. These questionnaires will take about 30 minutes in total to complete at each session. You will also be asked to complete a breath test and to provide a saliva sample. The breath test and the saliva sample will help the researchers find out how much you have smoked.

You will also be called on 2 occasions after your quit day, and you will be asked some questions about your smoking. Each phone call will last about 15 minutes. During the study, a staff member will meet with you for 10 to 20 minutes and help you to try and quit. You will meet with the staff member at each of the laboratory sessions. Every participant will receive the same help.

Some participants will be asked to carry a handheld computer (PDA) around for 1 week after their quit day. The PDA will beep randomly about 4 times a day (random assessments). Participants will answer some questions about their mood and craving, and complete a computerized reaction time task. Each assessment takes about 5 minutes.

Participation in this study will be over after your final visit to USU, which will be 4 weeks after your quit day.

4. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

Up to 250 subjects are expected to take part in this study at USU.

5. AMOUNT OF TIME FOR YOU TO COMPLETE THE STUDY

If you are eligible, you will be part of this study for about 7 weeks.

ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

Civilians and military personnel may be paid for participation in this study. Payments will be made after each visit, as described above.

Civilians (non-federal). You will receive \$25 for completing the orientation (the first session). You will also receive \$50 for completing each laboratory session. You will receive compensation after each session. You will also receive \$15 for each telephone assessment that you complete, and you will receive this at the final laboratory session. Participants who carry around the PDA for a week will receive \$2.50 for each random assessment that they complete.

Civilians (federal). You will only receive compensation for laboratory sessions/telephone assessments if those sessions occur during non-duty hours. In addition, if you wish to be compensated for participation during non-duty hours, you must file a request for outside activity. If the request is approved and the sessions occur during non-duty hours, payment will be made as follows. You will receive \$25 for completing the orientation (the first session). You will also receive \$50 for completing each laboratory session. You will receive compensation after each session. You will also receive \$15 for each telephone assessment that you complete (if those assessments occur during non-duty hours), and you will receive this at the final laboratory session. Federal civilians may participate in the PDA part of the study, but they can only be compensated for the PDA assessments that occur during non-duty hours.

Uniformed Personnel. You will only receive compensation for laboratory sessions if those sessions occur during non-duty hours. In addition, if you wish to be compensated for participation during non-duty hours, you must file a request for outside activity. If the request is approved and the sessions occur during non-duty hours, payment will be made as follows. You will receive \$25 for completing the orientation (the first session). You will also receive \$50 for completing each laboratory session. You will receive compensation after each session. You will also receive \$15 for each telephone assessment that you complete (if those assessments occur during non-duty hours), and you will receive this at the final laboratory session. Uniformed personnel may participate in the PDA part of the study, but they can only be compensated for the PDA assessments that occur during non-duty hours.

Please Note: Federal Civilians and Uniformed Personnel should inform their supervisors about the study for which they are volunteering whether or not they will receive compensation.

At the orientation session, if you are ineligible for the study because the breath test indicates that you have low levels of carbon monoxide in your breath, the orientation session will end right away and you will receive \$10 for your time and travel expenses. If you are ineligible for another reason, the session will last for a longer duration and you will receive \$25 for your time and travel expenses. Payments to ineligible participants follow the same rules as those written above for the eligible participants.

7. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

The expected risks or discomforts from being in this study are expected to be minimal. There are no known risks associated with the computerized evaluations. On 1 pre-quit session, you will arrive having not smoked on that day. You may experience symptoms of nicotine withdrawal, which include restlessness, difficulty concentrating, and/or mood changes. You will also smoke a cigarette at each of the pre-quit visits. Though smoking is considered bad for your health, your smoke intake is not likely to be increased by participating in this study. (Your smoke intake is likely to be decreased by participating in the study).

You may refuse to answer any question that makes you feel uncomfortable. If you have concerns after completing the questionnaires, you are encouraged to contact your doctor or the study chair.

If something in this research makes you uncomfortable or upset, you may choose to stop taking part in this research at any time without loss of benefits; you may contact the investigator for referral. If the investigators note any distress or anxiety associated with the research, you will receive referrals, if appropriate.

POSSIBLE BENEFITS FROM BEING IN THIS STUDY

You may benefit from this study because if you are able to quit, this may be very beneficial to your health. Future smokers may benefit from what is learned. The information we learn may help us learn to develop better smoking cessation programs.

However, no benefit can be guaranteed.

9. CONFIDENTIALITY/PRIVACY AND HOW YOUR IDENTITY AND YOUR RESEARCH RECORDS WILL BE MAINTAINED

All information you provide as part of this study will be confidential and will be protected to the fullest extent provided by law. Your responses to our interviews and questionnaires, as well as audio-taped sessions will be maintained in a locked filing cabinet in lab offices in the Department of Medical and Clinical Psychology. All records related to this study will be accessible to those persons directly involved in conducting this study and members of the USUHS Institutional Review Board (IRB), which provide oversight for protection of human research volunteers. In addition, the IRB at USUHS and other federal agencies that help protect people who are involved in research studies, may need to see the information you give us. Other than those groups, records from this study will be kept private to the fullest extent of the law. Scientific reports that come out of this study may include your ideas, but they will not use your name or identify you in any way.

10. CONDITIONS WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

The investigator may stop you from taking part in this study if being in the study is unsafe or dangerous to you or if you lose your right to receive medical care at military hospitals. The investigator may also stop you participating if you experience difficulty in following the procedures.

11. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND THE INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible; by leaving this study at any time, you in no way risk losing your right to medical care.

12. RECOURSE IN THE EVENT OF INJURY

If at any time you believe you have suffered an injury or illness as a result of participating in this research project, you should contact the Director of Human Research Protections Program at the Uniformed Services University of the Health Sciences, Bethesda, Maryland 20814-4799 at (301) 295-9534. This office can review the matter with you, can provide information about your rights as a subject, and may be able to identify resources available to you. If you believe the government or one of the government's employees (such as a military doctor) has injured you, a claim for damages (money) against the federal government (including the military) may be filed under the Federal Torts Claims Act. Information about judicial avenues of compensation is available from the University's General Counsel at (301) 295-3028.

CONTACT FOR QUESTIONS OR PROBLEMS

If you have questions about this research, you should contact Andrew J. Waters, Ph.D. the person in charge of the study. His phone number at USUHS is 301 295-9675. Even in the evening or on weekends, you can leave a message at that number. If you have questions about your rights as a research subject, you should call the Director of Human Research Protections Program at USUHS at (301) 295-9534. She is your representative and has no connection to the researcher conducting this study.

SIGNATURE OF RESEARCH PARTICIPANT OR LEGAL REPRESENTATIVE

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

Participant's Signature

Date

Participant's Printed Name

SIGNATURE OF INVESTIGATOR/RESEARCH TEAM MEMBER

You have explained the research to the participant, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

Investigator's/Research Team Member's Signature Date (must be the same as the participant's)

Investigator's/Research Team Member's Printed Name

SIGNATURE OF WITNESS

Your signature as witness is intended to attest that the information in the consent document and any other information was explained to and apparently understood by the participant, or the participant's legal representative, that questions and concerns were addressed and that informed consent was freely given.

Witness' Signature

Date (must be the same as the participant's)

Witness' Printed Name

Appendix E: Self-Report Measures

FAGERSTRÖM TEST FOR NICOTINE DEPENDENCE

	Within 5 minutes	6 to 30 minutes	31 to 60 minutes	After 60 minutes
1. How soon after you wake up do you smoke your <u>first</u> cigarette?			Yes	No
2. Do you find it difficult to refrain from smoking in places where it is forbidden, e.g., in church, at the library, in the cinema, etc.?			1st one in the A.M.	All others
3. Which cigarette would you hate to give up most?				
	10 or less	11-20	21-30	31 or more
4. How many cigarettes per day do you smoke?				
5. Do you smoke more frequently during the first hours after waking than the rest of the day?			Yes	No
6. Do you smoke if you are so ill that you are in bed most of the day?			Yes	No

QUESTIONNAIRE OF SMOKING URGES (BRIEF)

Questionnaire of Smoking Urges

	Strongly Disagree			Strongly Agree		
1. I have a desire for a cigarette.	0	1	2	3	4	5
2. Nothing would be better than smoking a cigarette.	0	1	2	3	4	5
3. If it were possible, I probably would smoke a cigarette.	0	1	2	3	4	5
4. I would control things better if I could smoke.	0	1	2	3	4	5
5. All I want is a cigarette.	0	1	2	3	4	5
6. I have an urge for a cigarette.	0	1	2	3	4	5
7. A cigarette would taste good.	0	1	2	3	4	5
8. I would do almost anything for a cigarette.	0	1	2	3	4	5
9. Smoking would make me less depressed.	0	1	2	3	4	5
10. I am going to smoke as soon as possible.	0	1	2	3	4	5

SUBJECTIVE ATTENTIONAL BIAS QUESTIONNAIRE

For each of the following items, please circle a number that best describes you.

- **During the past week, how often have you found your attention drawn to cigarettes?**

0	1	2	3	4
Not at all	A little bit	A moderate amount	A lot	An extreme amount

- **During the past week, how attractive have you found the sight of cigarettes?**

0	1	2	3	4
Not at all attractive	A little attractive	Moderately attractive	Very attractive	Extremely attractive

- **During the past week, how sensitive have you been to the smell of smoke?**

0	1	2	3	4
Not at all sensitive	A little sensitive	Moderately sensitive	Very sensitive	Extremely sensitive

- **During the past week, how attractive have you found the smell of smoke?**

0	1	2	3	4
Not at all attractive	A little attractive	Moderately attractive	Very attractive	Extremely attractive

- **During the past week, how often have you found yourself noticing people smoking?**

0	1	2	3	4
Not at all	A little bit	A moderate amount	A lot	An extreme amount

- **During the past week, how often have you found yourself staring at cigarettes and cigarette smoke?**

0	1	2	3	4
Not at all	A little bit	A moderate amount	A lot	An extreme amount

- **During the past week, how often have thoughts or images of smoking popped into you mind?**

0	1	2	3	4
Not at all	A little bit	A moderate amount	A lot	An extreme amount

- **During the past week, how attractive have thoughts or images of smoking been?**

0	1	2	3	4
Not at all attractive	A little attractive	Moderately attractive	Very attractive	Extremely attractive

SMOKING DIARY

Study ID: _____

Tobacco Use Record Form

Instructions for Participant:

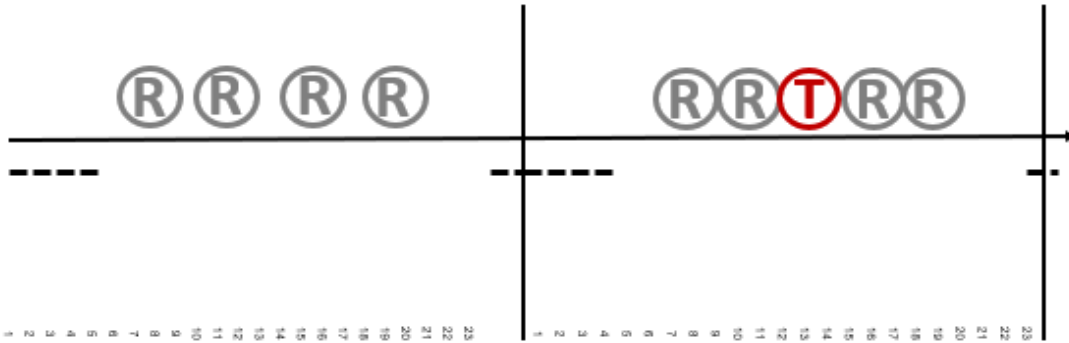
- Complete this form each day.
- Just before going to sleep, indicate how many cigarettes you have smoked that day.
- Be honest... Accurate information is important!

I agree to complete this form every night. I will provide information that is as accurate as possible.

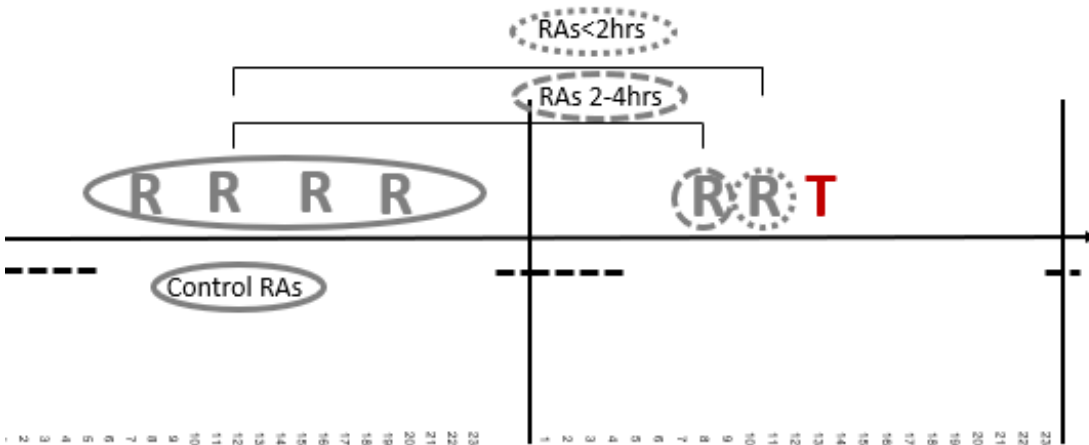
SIGNATURE AND DATE:

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week 1							
Week 2							
Week 3							

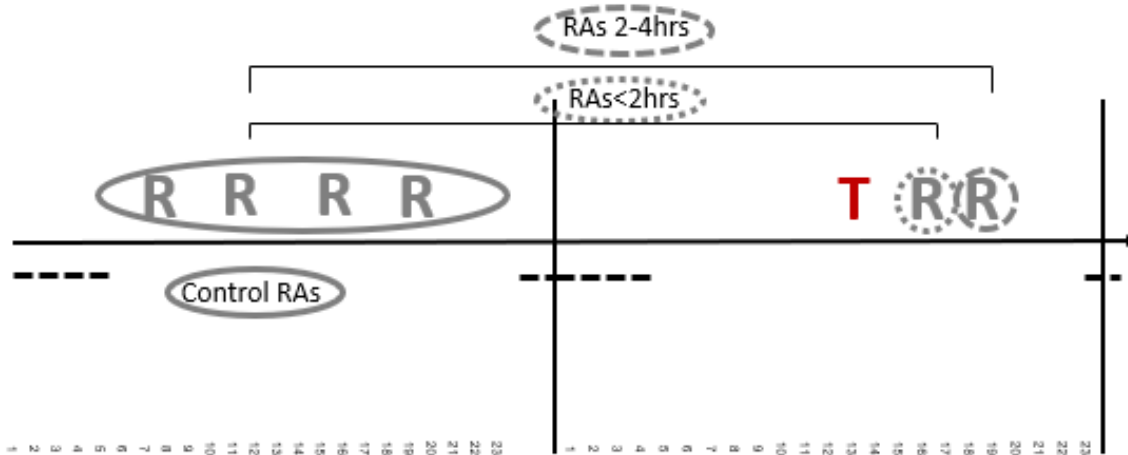
Appendix F: Visual Depiction of Specific Aims Analyses



Comparisons for Specific Aim 1



Comparisons for Specific Aim 2



Comparisons for Specific Aim 3

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